10560672restrict

agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:47:14 ON 11 JUL 2007

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:47:25 ON 11 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JUL 2007 HIGHEST RN 942116-98-5
DICTIONARY FILE UPDATES: 10 JUL 2007 HIGHEST RN 942116-98-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

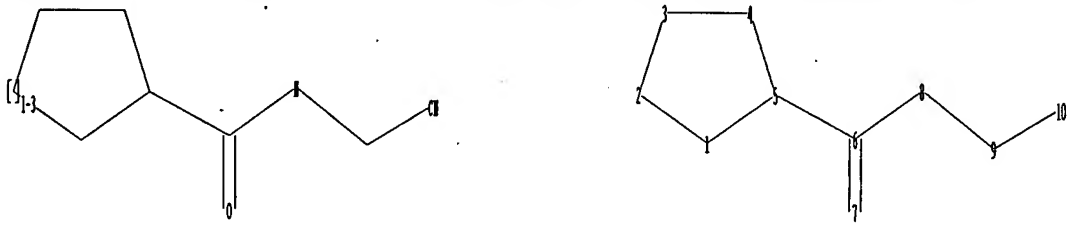
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10560672restrict.str



chain nodes :
6 7 8 10
ring nodes :
1 2 3 4 5
ring/chain nodes :
9
chain bonds :
5-6 6-7 6-8 8-9 9-10

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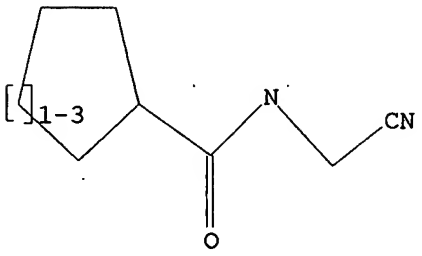
10560672restrict

ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-8 8-9
exact bonds :
5-6 9-10

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 16:47:49 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1045 TO ITERATE

100.0% PROCESSED 1045 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 18961 TO 22839
PROJECTED ANSWERS: 3206 TO 4914

L2 50 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 16:47:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 21815 TO ITERATE

100.0% PROCESSED 21815 ITERATIONS 4217 ANSWERS
SEARCH TIME: 00.00.01

L3 4217 SEA SSS FUL L1

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=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	172.10	172.31

FILE 'CAPLUS' ENTERED AT 16:47:56 ON 11 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 11 Jul 2007 VOL 147 ISS 3
FILE LAST UPDATED: 10 Jul 2007 (20070710/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 762 L3

=> d ibib abs hitstr 400-420

Karen Cheng

10560672restrict

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	112.08	284.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-16.38	-16.38

FILE 'REGISTRY' ENTERED AT 16:49:42 ON 11 JUL 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JUL 2007 HIGHEST RN 942116-98-5
DICTIONARY FILE UPDATES: 10 JUL 2007 HIGHEST RN 942116-98-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

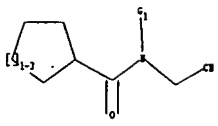
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

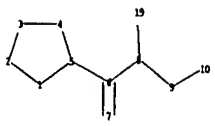
http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10560672restrict1.str

Karen Cheng

10560672restrict





chain nodes :
6 7 8 10 13 14 15 16 19
ring nodes :
1 2 3 4 5
ring/chain nodes :
9
chain bonds :
5-6 6-7 6-8 8-9 8-19 9-10 13-14 13-15 13-16
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5 6-7 6-8 8-9 8-19
exact bonds :
5-6 9-10 13-14 13-15 13-16

G1:H,[*1]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 19:CLASS

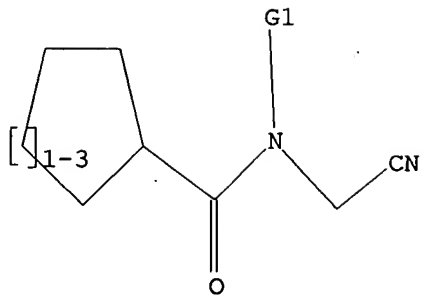
L5 STRUCTURE UPLOADED

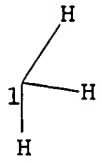
=> d

Karen Cheng

10560672restrict

L5 HAS NO ANSWERS
L5 STR





G1 H,[@1]

Structure attributes must be viewed using STN Express query preparation.

=> d his

(FILE 'HOME' ENTERED AT 16:47:14 ON 11 JUL 2007)

FILE 'REGISTRY' ENTERED AT 16:47:25 ON 11 JUL 2007
L1 STRUCTURE UPLOADED
L2 50 S L1
L3 4217 S L1 FULL

FILE 'CAPLUS' ENTERED AT 16:47:56 ON 11 JUL 2007
L4 762 S L3

FILE 'REGISTRY' ENTERED AT 16:49:42 ON 11 JUL 2007
L5 STRUCTURE UPLOADED

=> s l5 full sub = l3
FULL SUBSET SEARCH INITIATED 16:50:08 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED - 4217 TO ITERATE

100.0% PROCESSED 4217 ITERATIONS 3518 ANSWERS
SEARCH TIME: 00.00.01

L6 3518 SEA SUB=L3 SSS FUL L5

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

Karen Cheng

10560672restrict

FULL ESTIMATED COST	41.10	325.49

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-16.38

FILE 'CAPLUS' ENTERED AT 16:50:13 ON 11 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 11 Jul 2007 VOL 147 ISS 3
FILE LAST UPDATED: 10 Jul 2007 (20070710/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l6
L7 630 L6

=> d ibib abs hitstr 500-510

Karen Cheng

10560672restrict

=> fil reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	59.38	384.87

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.58	-24.96

FILE 'REGISTRY' ENTERED AT 16:51:52 ON 11 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 10 JUL 2007 HIGHEST RN 942116-98-5
DICTIONARY FILE UPDATES: 10 JUL 2007 HIGHEST RN 942116-98-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10560671restrict2.str

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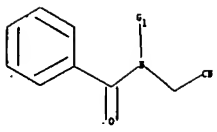
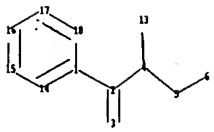
10560672restrict





chain nodes :
2 3 4 6 7 8 9 10 13
ring nodes :
1 14 15 16 17 18
ring/chain nodes :
5
chain bonds :
1-2 2-3 2-4 4-5 4-13 5-6 7-8 7-9 7-10
ring bonds :
1-14 1-18 14-15 15-16 16-17 17-18
exact/norm bonds :
2-3 2-4 4-5 4-13
exact bonds :
1-2 5-6 7-8 7-9 7-10
normalized bonds :
1-14 1-18 14-15 15-16 16-17 17-18

G1:H,[*1]

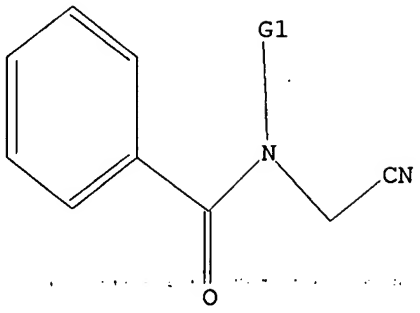
Match level :
1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 13:CLASS 14:Atom 15:Atom 16:Atom 17:CLASS 18:Atom

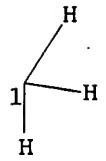
Karen Cheng

10560672restrict

L8 STRUCTURE UPLOADED

=> d
L8 HAS NO ANSWERS
L8 STR





G1 H,[@1]

Structure attributes must be viewed using STN Express query preparation.

=> d his

(FILE 'HOME' ENTERED AT 16:47:14 ON 11 JUL 2007)

FILE 'REGISTRY' ENTERED AT 16:47:25 ON 11 JUL 2007
L1 STRUCTURE UPLOADED
L2 50 S L1
L3 4217 S L1 FULL

FILE 'CAPLUS' ENTERED AT 16:47:56 ON 11 JUL 2007
L4 762 S L3

FILE 'REGISTRY' ENTERED AT 16:49:42 ON 11 JUL 2007
L5 STRUCTURE UPLOADED
L6 3518 S L5 FULL SUB=L3

FILE 'CAPLUS' ENTERED AT 16:50:13 ON 11 JUL 2007
L7 630 S L6

FILE 'REGISTRY' ENTERED AT 16:51:52 ON 11 JUL 2007
L8 STRUCTURE UPLOADED

=> s l8 full sub=l6
FULL SUBSET SEARCH INITIATED 16:52:38 FILE 'REGISTRY'

Karen Cheng

10560672restrict

FULL SUBSET SCREEN SEARCH COMPLETED - 3518 TO ITERATE

100.0% PROCESSED 3518 ITERATIONS 2344 ANSWERS
SEARCH TIME: 00.00.01

L9 2344 SEA SUB=L6 SSS FUL L8

=> s l6 not l9
L10 1174 L6 NOT L9

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	41.55	426.42

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-24.96

FILE 'CAPLUS' ENTERED AT 16:52:55 ON 11 JUL 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 11 Jul 2007 VOL 147 ISS 3
FILE LAST UPDATED: 10 Jul 2007 (20070710/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l10
L11 70 L10

=> d ibib abs hitstr 50-60

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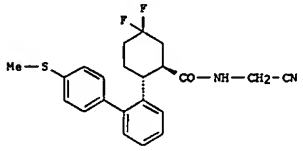
=> d ibib abs hitstr tot

Karen Cheng

L11 ANSWER 1 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:526104 CAPLUS
TITLE: β-Substituted cyclohexanecarboxamide cathepsin K inhibitors: Modification of the 1,2-disubstituted aromatic core
AUTHOR(S): Robichaud, Joeel; Bayly, Christopher I.; Black, W. Cameron; Desmarais, Sylvie; Leger, Serge; Masse, Frederic; McKay, Daniel J.; Oballa, Renata M.; Paquet, Julie; Percival, M. David; Truchon, Jean-Francois; Wesolowski, Gregg; Crane, Sheldon N.
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Kirkland, QC, H9H 3L1, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2007), 17(11), 3146-3151
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

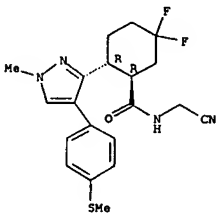
AB Further SAR study around the central 1,2-disubstituted Ph of the previously disclosed Cat K inhibitor (-)-1 (I) has demonstrated that the solvent exposed P2-P3 linker can be replaced by various 5- or 6-membered heteroarom. rings. While some potency loss was observed in the 6-membered heteroarom. series (IC50 = 1 nM for pyridine-linked 4 vs 0.5 nM for phenyl-linked (±)-1), several inhibitors showed a significantly decreased shift in the bone resorption functional assay (10-fold for pyridine 4 vs 53-fold for (-)-1). Though this shift was not reduced in the 5-membered heteroarom. series, potency against Cat K was significantly improved for thiazole 9 (IC50 = 0.2 nM) as was the pharmacokinetic profile of N-Me pyrazole 10 over our lead compound (-)-1.

IT 819858-04-3P 941608-61-3P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β-substituted cyclohexanecarboxamide cathepsin K inhibitors)

RN 819858-04-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[1-methyl-4-[4-

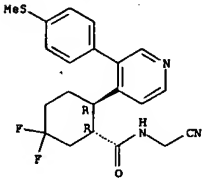
L11 ANSWER 1 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(methylthio)phenyl]-1H-pyrazol-3-yl]-, (1R,2R)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 941608-61-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[3-[4-(methylthio)phenyl]-4-pyridinyl]-, (1R,2R)-rel- (CA INDEX NAME)

Relative stereochemistry.

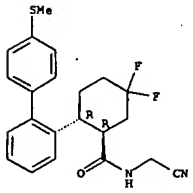


IT 819858-00-9
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PRP (Properties); USES (Uses)
(β-substituted cyclohexanecarboxamide cathepsin K inhibitors)

RN 819858-00-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

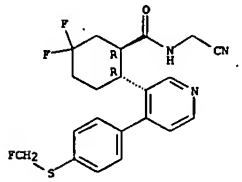
L11 ANSWER 1 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 941608-60-2P 941608-62-4P 941608-63-5P
941608-64-6P 941608-65-7P 941608-66-8P
941608-67-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β-substituted cyclohexanecarboxamide cathepsin K inhibitors)

RN 941608-60-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4-[4-[(fluoromethyl)thio]phenyl]-3-pyridinyl]-, (1R,2R)-rel- (CA INDEX NAME)

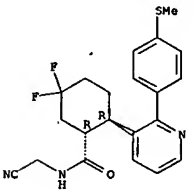
Relative stereochemistry.



RN 941608-62-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[2-[4-(methylthio)phenyl]-3-pyridinyl]-, (1R,2R)-rel- (CA INDEX NAME)

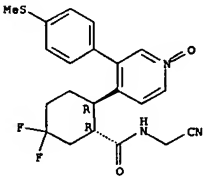
Relative stereochemistry.

L11 ANSWER 1 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



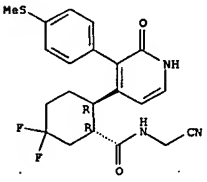
RN 941608-63-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[3-[4-(methylthio)phenyl]-1-oxido-4-pyridinyl]-, (1R,2R)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 941608-64-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[1,2-dihydro-3-[4-(methylthio)phenyl]-2-oxo-4-pyridinyl]-5,5-difluoro-, (1R,2R)-rel- (CA INDEX NAME)

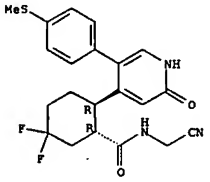
Relative stereochemistry.



Karen Cheng

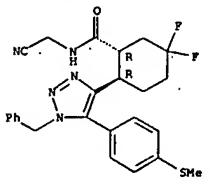
L11 ANSWER 1 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 941608-65-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[1,2-dihydro-5-[4-(methylthio)phenyl]-2-oxo-4-pyridinyl]-5,5-difluoro-, (1R,2R)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 941608-66-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[5-[4-(methylthio)phenyl]-1-(phenylmethyl)-1H-1,2,3-triazol-4-yl]-, (1R,2R)-rel- (CA INDEX NAME)

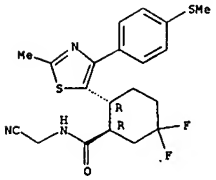
Relative stereochemistry.



RN 941608-67-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[2-methyl-4-[4-(methylthio)phenyl]-5-thiazolyl]-, (1R,2R)-rel- (CA INDEX NAME)

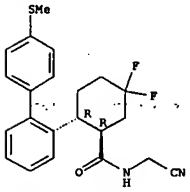
Relative stereochemistry.

L11 ANSWER 1 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



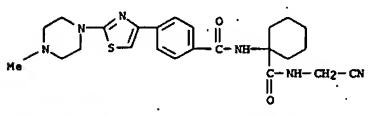
IT 875142-78-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-substituted cyclohexanecarboxamide cathepsin K inhibitors)
RN 875142-78-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (CA INDEX NAME)

Relative stereochemistry.



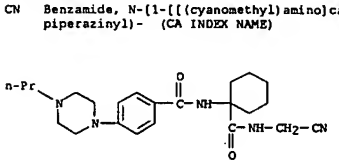
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:519392 CAPLUS
TITLE: MSE with mass defect filtering for in vitro and in vivo metabolite identification
AUTHOR(S): Bateman, Kevin P.; Castro-Perez, Jose; Wrona, Mark; Shockcor, John P.; Yu, Kate; Oballa, Renata; Nicoll-Griffith, Deborah A.
CORPORATE SOURCE: Merck Frosst Canada Ltd., Kirkland, QC, H9H 3L1, Can.
SOURCE: Rapid Communications in Mass Spectrometry (2007), 21(9), 1485-1496
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Metabolite identification studies involve the detection and structural characterization of the biotransformation products of drug candidates. These expts. are necessary throughout the drug discovery and development process. The use of high-resolution chromatog. and high-resolution mass spectrometry together with data processing using mass defect filtering is described for in vitro and in vivo metabolite identification studies. Data collection was done using UPLC coupled with an orthogonal hybrid quadrupole time-of-flight mass spectrometer. This exptl. approach enabled the use of MSE data collection (where E represents collision energy) which has previously been shown to be a powerful approach for metabolite identification studies. Post-acquisition processing with a prototype mass defect filtering program was used to eliminate endogenous interferences in the study samples, greatly enhancing the discovery of metabolites. The ease of this approach is illustrated by results showing the detection and structural characterization of metabolites in plasma from a preclin. rat pharmacokinetic study.
IT INDEXING IN PROGRESS
IT 294623-49-7, L-006235
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(MSE with mass defect filtering for in vitro and in vivo metabolite identification)
RN 294623-49-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:388646 CAPLUS
DOCUMENT NUMBER: 146:414126
TITLE: Emerging roles of cysteine cathepsins in disease and their potential as drug targets
AUTHOR(S): Vasiljeva, Olga; Reinheckel, Thomas; Peters, Christoph; Turk, Dusan; Turk, Vito; Turk, Boris
CORPORATE SOURCE: Institut fuer Molekulare Medizin und Zellforschung, Albert-Ludwigs-Universitaet Freiburg, Freiburg, Germany
SOURCE: Current Pharmaceutical Design (2007), 13(4), 387-403
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The general view on Cys cathepsins, which were long believed to be primarily involved in intracellular protein turnover, has dramatically changed in last 10 to 15 years. The discovery of new cathepsins, such as cathepsins K, V, X, F and O, and their tissue distribution suggested that at least some of them are involved in very specific cellular processes. Moreover, gene ablation expts. revealed that cathepsins play a vital role in numerous physiol. processes, such as antigen processing and presentation, bone remodeling, prohormone processing and wound healing. Their involvement in several pathologies, including osteoporosis, rheumatoid arthritis, osteoarthritis, bronchial asthma and cancer were also confirmed and today several of them were validated as relevant targets for therapies. Compds. targeting cathepsins S and K are already in clin. evaluation, whereas others are in exptl. phases. The cathepsin K inhibitor AAE-581 (balicatib) as the most advanced of them passed Phase II clin. trials in 2005. In this review, we discuss the current view on cathepsins as an emerging group of targets for several diseases and the development of cathepsin K and S inhibitors for treatment of osteoporosis and various immune disorders.
IT 354813-19-7, Balicatib
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cys cathepsins in physiol. and diseases, and potential as drug targets)
RN 354813-19-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)



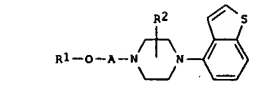
REFERENCE COUNT: 223 THERE ARE 223 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:257347 CAPLUS
DOCUMENT NUMBER: 146:316939
TITLE: Preparation of benzo[b]thiophen-4-yl-piperazine and related compounds as antipsychotic agents for the treatment of mental disorders
INVENTOR(S): Yamashita, Hiroshi; Matsubara, Jun; Oshima, Kunio; Kuroda, Hideaki; Ito, Nobuaki; Miyamura, Shin; Shimizu, Satoshi; Tanaka, Tatsuyoshi; Taira, Shinichi; Kondo, Kazumi; Itotani, Motohiro; Bando, Masahiko; Fukushima, Tae; Oshiro, Yasuo; Takahashi, Haruka; Sakurai, Yohji; Kuroda, Takeshi; Shimada, Jun; Maeda, Kenji; Tadori, Yoshihiro; Amada, Naoki; Akazawa, Hitomi; Yamashita, Junko; Mori, Atsushi; Uwahodo, Yasufumi; Masumoto, Takumi; Sugino, Haruhiko; Kikuchi, Tetsuro; Hashimoto, Kazuya
PATENT ASSIGNEE(S): Otsuka Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 686pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

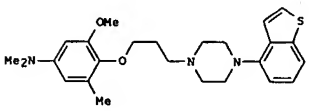
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007026959	A2	20070308	WO 2006-JP317704	20060831
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
JP 2007091733	A	20070412	JP 2006-235401	20060831
PRIORITY APPLN. INFO.:			JP 2005-251055 A	20050831
OTHER SOURCE(S):	MARPAT 146:316939			

GI

L11 ANSWER 4 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I



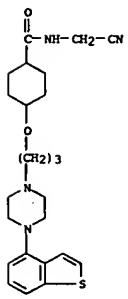
II

AB Title compds. I [R1 = cycloalkyl, (un)substituted aryl, heterocyclyl; R2 = H or lower alkyl; A = lower alkylene or lower alkenylene], and their pharmaceutically acceptable salts, are prepared and disclosed as antipsychotic agents for the treatment of mental disorders. Thus, e.g., II·HCl was prepared via nucleophilic substitution of [4-(3-chloropropoxy)-3-methoxy-5-methylphenyl]-carbamic acid tert-Bu ester (preparation given) with 1-benzo[b]thiophen-4-yl-piperazine hydrochloride (preparation given) followed by deprotection and dimethylation. Binding assays were used to determine Ki values for I, e.g., II·HCl demonstrated Ki values of 0.4 nM in Dopamine D2 receptor and 5.9 nM in Serotonin 5-HT2A receptor. Serotonin uptake inhibitory activity of II·HCl was also determined as 95.3%. The invention compds. may be widely used in the treatment and prevention of mental disorders including central nervous system disorders, while demonstrating no side effects.

IT 928242-97-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzo[b]thiophen-4-yl-piperazine and related compds. as antipsychotic agents for the treatment of mental disorders)

RN 928242-97-1 CAPLUS
CN Cyclohexanecarboxamide, 4-[3-(4-benzo[b]thien-4-yl-1-piperazinyl)propoxy]-N-(cyanomethyl)- (CA INDEX NAME)

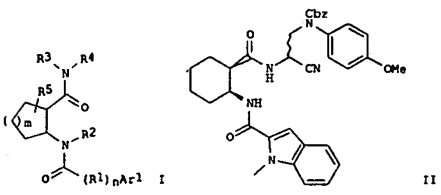
L11 ANSWER 4 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L11 ANSWER 5 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:150949 CAPLUS
DOCUMENT NUMBER: 146:229179
TITLE: Preparation of (hetero)arylcarbonylaminocycloalkylcarboxamides as cathepsin K inhibitors.
INVENTOR(S): Bamberg, Joe Timothy; Gabriel, Tobias
PATENT ASSIGNEE(S): F. Hoffmann-La Roche AG, Switz.
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014839	A2	20070208	WO 2006-EP64306	20060717
WO 2007014839	A3	20070426		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
US 2007032484	A1	20070208	US 2006-493208	20060725
PRIORITY APPLN. INFO.:			US 2005-702937P P	20050727
OTHER SOURCE(S):	MARPAT 146:229179			

GI



I II

AB Title compds. [I; m = 1-3; n = 0, 1; Ar1 = (bi)aryl, heteroaryl; R1 = alkylene; R2, R3, R5 = H, alkyl; R4 = aralkyl, cycloalkyl, heterocyclyl, heteroaralkyl, etc.], were prepared for treatment of osteoporosis, tumor metastasis, unstable angina, and plaque rupture (no data). Thus, title compound (II) was prepared in 81% yield as a separable mixture of isomers via coupling of the corresponding acid and amine in DMF using EDCI hydrochloride, HOBt, and N-methylmorpholine.

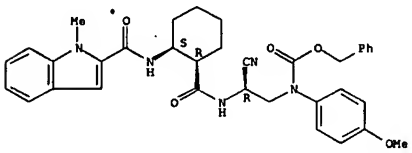
L11 ANSWER 5 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

IT 924298-88-4P 924298-89-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (hetero)arylcarbonylaminocycloalkylcarboxamides as cathepsin K inhibitors)

RN 924298-88-4 CAPLUS

CN Carbamic acid, N-[(2R)-2-cyano-2-[[[(1R,2S)-2-[[(1-methyl-1H-indol-2-yl)carbonyl]amino]cyclohexyl]carbonyl]amino]ethyl]-N-(4-methoxyphenyl)-, phenylmethyl ester (CA INDEX NAME)

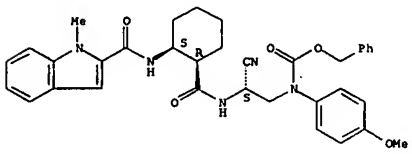
Absolute stereochemistry.



RN 924298-89-5 CAPLUS

CN Carbamic acid, N-[(2S)-2-cyano-2-[[[(1R,2S)-2-[[(1-methyl-1H-indol-2-yl)carbonyl]amino]cyclohexyl]carbonyl]amino]ethyl]-N-(4-methoxyphenyl)-, phenylmethyl ester (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 6 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

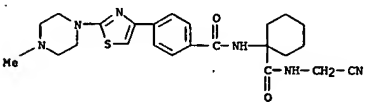
ACCESSION NUMBER: 2007:129940 CAPLUS
DOCUMENT NUMBER: 146:350583
TITLE: A generally applicable method for assessing the electrophilicity and reactivity of diverse nitrile-containing compounds
AUTHOR(S): Oballa, Renata M.; Truchon, Jean-Francois; Bayly, Christopher I.; Chauret, Nathalie; Day, Stephen; Crane, Sheldon; Berthelette, Carl
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, H9H 3L1, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2007), 17(4), 998-1002
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nitrile-based inhibitors of cathepsin K have been known for some time and mechanism-of-action studies have demonstrated that cysteinyl proteases interact with nitriles in a reversible fashion. Three main classes of nitrile-containing inhibitors have been published in the cathepsin K field: (i) cyanamides, (ii) aromatic nitriles, and (iii) aminoacetonitriles. A computational approach was used to calculate the theor. reactivities of diverse nitriles and this was found to correlate with their extent of reactivity with free cysteine. Moreover, there is a tentative link between high reactivity with cysteine and the potential to lead to irreversible covalent binding to proteins.

IT 294623-49-7, L-006235 354813-19-7, Balicatib
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); BIOL (Biological study); PROC (Process)
(method for assessing electrophilicity and reactivity of diverse nitrile-containing compds.)

RN 294623-49-7 CAPLUS

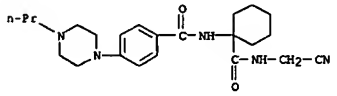
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)



RN 354813-19-7 CAPLUS

CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)

L11 ANSWER 6 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:61234 CAPLUS
DOCUMENT NUMBER: 146:184461
TITLE: Preparation of as azolopyridines as inhibitors of JAK3 janus protein kinase.
INVENTOR(S): Inoue, Takayuki; Tojo, Takashi; Morita, Masataka; Nakajima, Yutaka; Hatanaka, Keiko; Shirakami, Shohei; Sasaki, Hiroshi; Tanaka, Akira; Takahashi, Fumie; Mukoyoshi, Koichiro; Higashi, Yasuyuki; Okimoto, Akira; Hondo, Takeshi; Sawada, Hitoshi
PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan
SOURCE: PCT Int. Appl., 260pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007007919	A2	20070118	WO 2006-JP314326	20060713
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2005-698928P P 20050714
JP 2005-378858 A 20051228

OTHER SOURCE(S): MARPAT 146:184461

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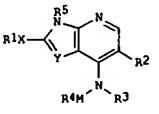
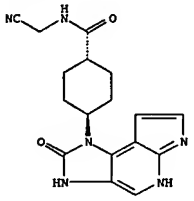


AB Title compds. [I; R1 = H, (substituted) alkyl, aryl; X = bond, NH, O; R2 = H, substituent; R3, R5 = H, alkyl; R4 = (substituted) cycloalkyl, heterocycloalkyl, alkyl, acyl, heteroaryl; M = (CH2)n; n = 0-4; Y = N, CR7; R7 = H, NO2, cyano, amino, halo, acyl, (substituted) alkyl; R2R3 = NR6CO; R6 = H, (substituted) alkyl; R3R4 = (substituted) alkylene; with provisos], were prepared Thus, Et 4-chloro-1H-pyrrolo[2,3-b]pyridine-5-carboxylate (preparation given) and (1S,2R)-2-methylcyclohexanamine were refluxed with diisopropylethylamine in BuOH in a sealed tube at 160° under microwave irradiation to give Et 4-[methyl[(1S,2R)-2-methylcyclohexyl]amino]-1H-pyrrolo[2,3-b]pyridine-5-carboxylate. The latter inhibited JAK3 by >50% at 10-5 M.

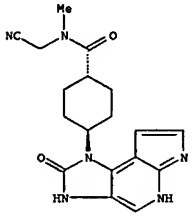
L11 ANSWER 7 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
IT 920961-20-2P 920961-24-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of as azolopyridines as inhibitors of JAK3 janus protein kinase)
RN 920961-20-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-4-(3,6-dihydro-2-oxoimidazo[4,5-d]pyrrolo[2,3-b]pyridin-1(2H)-yl)-, trans- (CA INDEX NAME)

Relative stereochemistry.



RN 920961-24-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-4-(3,6-dihydro-2-oxoimidazo[4,5-d]pyrrolo[2,3-b]pyridin-1(2H)-yl)-N-methyl-, trans- (CA INDEX NAME)

Relative stereochemistry.

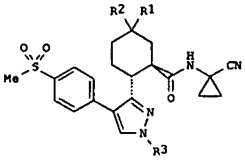


L11 ANSWER 8 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:34484 CAPLUS
DOCUMENT NUMBER: 146:142640
TITLE: 2-(4-Arylpyrazol-3-yl)cyclohexanecarboxamides as cathepsin cysteine protease inhibitors and their preparation, pharmaceutical compositions, and use in the treatment of bone resorption diseases
INVENTOR(S): Black, Cameron; Crane, Sheldon; Oballa, Renata; Robichaud, Joel
PATENT ASSIGNEE(S): Merck Frosst Canada Ltd., Can.
SOURCE: PCT Int. Appl., 43pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007003056	A1	20070111	WO 2006-CA1104	20060705

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-696970P P 20050706
OTHER SOURCE(S): MARPAT 146:142640
GI

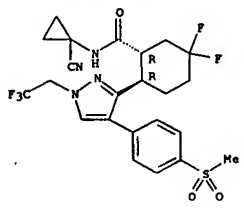


I

AB This invention relates to a class of compds., represented by the formula I, which are cysteine protease inhibitors, including but not limited to, inhibitors of cathepsin K, L, S and B. Compds. of formula I wherein R1

L11 ANSWER 8 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
and R2 are halo; R3 is H, C1-6 (halo)alkyl, C3-6 cycloalkyl and (hetero)aryl; and their pharmaceutically acceptable salts, stereoisomers and N-oxides, thereof are claimed. These compds. are useful for treating diseases in which inhibition of bone resorption is indicated, such as osteoporosis, osteoarthritis and rheumatoid arthritis. Example compd. I (R1 = R2 = F; R3 = CH2CF3) was prepd. by olefination of benzyloxyacetaldehyde with {2-[(4R)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl]-2-oxoethyl}phosphonate; the resulting (4R)-4-benzyl-3-[(2E)-4-(benzyloxy)but-2-enoyl]-1,3-oxazolidin-2-one underwent Diels-Alder cyclization with 2-(trimethylsilyloxy)-1,3-butadiene to give (4R)-4-benzyl-3-[[(1R,2R)-2-[(benzyloxy)methyl]-4-oxocyclohexyl]carbonyl]-1,3-oxazolidin-2-one, which underwent fluorination to give the corresponding difluorocyclohexane deriv., which underwent Suzuki cross-coupling with hydride redn. to give [(1R,2R)-2-[(benzyloxy)methyl]-4,4-difluorocyclohexyl]methanol, which underwent oxidn. to the corresponding aldehyde, which reacted with Et [4-(methylthio)phenyl]acetate to give Et 3-[2-[(benzyloxy)methyl]-4,4-difluorocyclohexyl]-3-hydroxy-2-[4-(methylthio)phenyl]propanoate, which underwent oxidn. to give the 3-oxopropanoate deriv., which underwent cyclization to give the corresponding 1-(trifluoroethyl)-1H-pyrazol-5-ol, which underwent sulfonylation, to give the corresponding pyrazol-5-yl triflate deriv., which underwent double hydrogenation to give [(1R,2R)-5,5-difluoro-2-[4-(methylsulfonyl)phenyl]-1-(2,2,2-trifluoroethyl)-1H-pyrazol-3-yl]cyclohexyl]methanol, which underwent oxidn. and amidation with 1-aminocyclopropanecarbonitrile hydrochloride to give compd. I. All the invention compds. were evaluated for their cathepsin cysteine protease inhibitory activity. These compds. may be useful in the treatment of bone resorption diseases.
IT 919109-75-4P 919109-76-5P 919109-77-6P
919109-78-7P 919109-79-8P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of arylpyrazolylcyclohexanecarboxamides as cysteine protease inhibitors useful in disease treatment requiring inhibition of bone resorption)
RN 919109-75-4 CAPLUS
CN Cyclohexanecarboxamide, N-(1-cyanocyclopropyl)-5,5-difluoro-2-[4-[4-(methylsulfonyl)phenyl]-1-(2,2,2-trifluoroethyl)-1H-pyrazol-3-yl]-, (1R,2R)- (CA INDEX NAME)

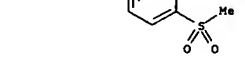
Absolute stereochemistry.



RN 919109-76-5 CAPLUS

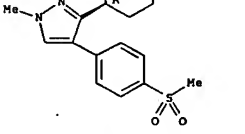
L11 ANSWER 8 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Cyclohexanecarboxamide, 5,5-dichloro-N-(1-cyanocyclopropyl)-2-[4-[4-(methylsulfonyl)phenyl]-1-(2,2,2-trifluoroethyl)-1H-pyrazol-3-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 919109-77-6 CAPLUS
CN Cyclohexanecarboxamide, N-(1-cyanocyclopropyl)-5,5-difluoro-2-[1-methyl-4-[4-(methylsulfonyl)phenyl]-1H-pyrazol-3-yl]-, (1R,2R)- (CA INDEX NAME)

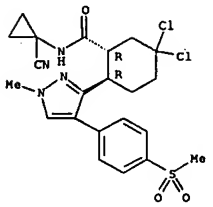
Absolute stereochemistry.



RN 919109-78-7 CAPLUS
CN Cyclohexanecarboxamide, 5,5-dichloro-N-(1-cyanocyclopropyl)-2-[1-methyl-4-[4-(methylsulfonyl)phenyl]-1H-pyrazol-3-yl]-, (1R,2R)- (CA INDEX NAME)

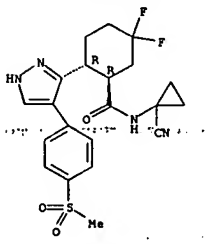
Absolute stereochemistry.

L11 ANSWER 8 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 919109-79-8 CAPLUS
CN Cyclohexanecarboxamide, N-(1-cyanocyclopropyl)-5,5-difluoro-2-[4-[4-(methylsulfonyl)phenyl]-1H-pyrazol-3-yl]-, (1R,2R)- (CA INDEX NAME)

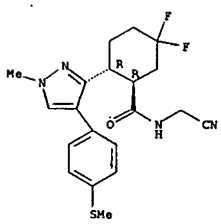
Absolute stereochemistry.



IT 919110-00-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of arylpyrazolylcyclohexanecarboxamides as
cysteine protease inhibitors useful in disease treatment requiring inhibition of bone resorption)
RN 919110-00-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[1-methyl-4-[4-(methylthio)phenyl]-1H-pyrazol-3-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.

L11 ANSWER 8 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

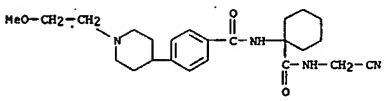
L11 ANSWER 9 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:937462 CAPLUS
DOCUMENT NUMBER: 145:465162
TITLE: Substrate mapping and inhibitor profiling of falcipain-2, falcipain-3 and berghepain-2: Implications for peptidase anti-malarial drug discovery
AUTHOR(S): Ramjee, Manoj K.; Flinn, Nicholas S.; Pemberton, Tracy P.; Quibell, Martin; Wang, Yikang; Watts, John P.
CORPORATE SOURCE: Amura Therapeutics Limited, Horizon Park, Comberton, CB3 7AJ, UK
SOURCE: Biochemical Journal (2006), 399(1), 47-57
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Plasmodium falciparum cysteine peptidases FP-2 (falcipain-2) and FP-3 (falcipain-3), members of the papain-like CAC1 family, are essential hemoglobinases and are therefore potential antimalarial drug targets. To facilitate a rational drug discovery program, in the current study the authors analyzed the synthetic substrate and model inhibitor profiles of FP-2 and FP-3 as well as BP-2 (berghepain-2), an ortholog from the rodent parasite Plasmodium berghei. With respect to substrate catalysis, FP-2 exhibited a promiscuous substrate profile based around a consensus nonprimeside motif, FP-3 was somewhat more restricted and BP-2 was comparatively specific. Substrate turnover for FP-2 was driven by a basic or acidic P1 residue, whereas for FP-3 turnover occurred predominately through a basic P1 residue only, and for BP-2, turnover was again mainly through a basic P1 residue for some motifs and surprisingly a glycine in the P1 position for other motifs. Within these P1 binding elements, addnl. recognition motifs were observed with subtle nuances that switched substrate turnover on or off through specific synergistic combinations. The peptidases were also profiled against reversible and irreversible cysteine peptidase inhibitors. The results reiterated the contrasting kinetic behavior of each peptidase as observed through the substrate screens.
The results showed that the substrate and inhibitor preferences of BP-2 were markedly different from those of FP-2 and FP-3. When FP-2 and FP-3 were compared to each other they also displayed similarities and some significant differences. In conclusion, the in vitro data highlights the current difficulties faced by a peptidase directed antimalarial medicinal chemical program where compds. need to be identified with potent activity against at least three peptidases, each of which displays distinct biochem. traits.

IT 354813-34-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substrate mapping and inhibitor profiling of falcipain-2, falcipain-3 and berghepain-2 and implications for peptidase anti-malarial drug discovery)
RN 354813-34-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[1-(2-methoxyethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

L11 ANSWER 9 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



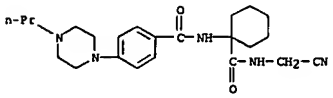
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:735916 CAPLUS
DOCUMENT NUMBER: 145:159867
TITLE: Cathepsin K inhibitors for the treatment of obesity and obesity-related disorders
INVENTOR(S): Percival, Michael David
PATENT ASSIGNEE(S): Merck Frosst Canada Ltd., Can.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006076796	A1	20060727	WO 2006-CA54	20060117

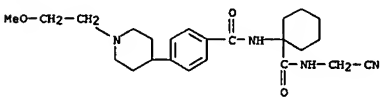
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-644926P P 20050119
OTHER SOURCE(S): MARPAT 145:159867
AB The invention relates to the treatment of obesity, the treatment of obesity-related disorders, prevention of weight gain, prevention of weight regain or for weight maintenance, by the use of a cathepsin K inhibitor as active ingredient, alone or in conjunction with other anti-obesity agents. The invention also relates to pharmaceutical compns. comprising cathepsin K inhibitors as active ingredients, pharmaceutically acceptable carriers or excipients, and optionally one or more anti-obesity agents.
IT 354813-19-7 354813-34-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cathepsin K inhibitors for treatment of obesity and obesity-related disorders)
RN 354813-19-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)



L11 ANSWER 10 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 354813-34-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[1-(2-methoxyethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



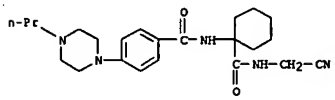
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:733104 CAPLUS
DOCUMENT NUMBER: 145:159834
TITLE: Cathepsin K inhibitors and atherosclerosis
INVENTOR(S): Percival, Michael David
PATENT ASSIGNEE(S): Merck Frosst Canada Ltd., Can.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

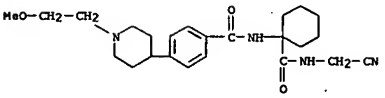
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006076797	A1	20060727	WO 2006-CA55	20060117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-644938P P 20050119
OTHER SOURCE(S): MARPAT 145:159834
AB This invention relates to a genus of compds., such as N1-(1-cyanocyclopropyl)-4-fluoro-N2-[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfinyl)-1,1'-biphenyl-4-yl]ethyl]-L-leucinamide or N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propylpiperazin-1-yl)benzamide, which are inhibitors of cathepsin K. These compds. are useful for treating or preventing atherosclerosis and atherosclerotic cardiovascular disease.
IT 354813-19-7 354813-34-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cathepsin K inhibitors and treatment of atherosclerosis and atherosclerotic cardiovascular diseases and combination with other agents)
RN 354813-19-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)



L11 ANSWER 11 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RN 354813-34-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[1-(2-methoxyethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

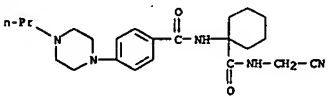
Karen Cheng

L11 ANSWER 12 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:605212 CAPLUS
DOCUMENT NUMBER: 145:46277
TITLE: Preparation of novel salts and modifications of N-[1-(cyanomethylcarbamoyl)cyclohexyl]-4-(4-propylpiperazin-1-yl)benzamide
INVENTOR(S): Pfeffer, Sabine; Nobs, Frederic; Karpinski, Piotr H.
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006063762	A1	20060622	WO 2005-EP13296	20051212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: GB 2004-27380 A 20041214
AB The invention relates to N-[1-(cyanomethylcarbamoyl)cyclohexyl]-4-(4-propylpiperazin-1-yl)benzamide (I) salts and modifications for use in the manufacture of pharmaceutical prepns. X-ray powder diffraction and DSC data were determined for crystalline modifications of I hydrogen maleate and its methanol solvate.
IT 354813-19-7
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation, X-ray powder diffraction, and DSC of [(cyanomethylcarbamoyl)cyclohexyl](propylpiperazinyl)benzamide hydrogen maleate)
RN 354813-19-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)

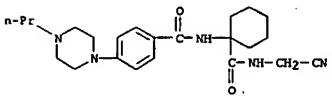


L11 ANSWER 12 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

IT 889858-57-5P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, X-ray powder diffraction, and DSC of [(cyanomethylcarbamoyl)cyclohexyl](propylpiperazinyl)benzamide hydrogen maleate)
RN 889858-57-5 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

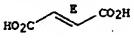
CRN 354813-19-7
CMF C23 H33 N5 O2



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



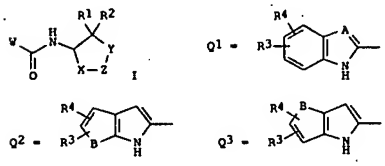
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:489919 CAPLUS
DOCUMENT NUMBER: 145:8021
TITLE: Preparation of chloroindolecarboxamides as glycogen phosphorylase inhibitors
INVENTOR(S): Sher, Philip M.; Wu, Gang; Meng, Wei; Nirschl, Alexandra A.; Washburn, William N.; Stouch, Terry
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006111413	A1	20060525	US 2005-273167	20051114
WO 2006055463	A2	20060526	WO 2005-US41098	20051114
WO 2006055463	A3	20061228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

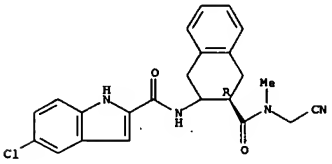
PRIORITY APPLN. INFO.: US 2004-628065P P 20041115
OTHER SOURCE(S): MARPAT 145:8021
GI



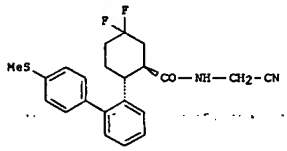
AB Title compds. [I; A = CH, N; B = O, S; W = Q1, Q2, Q3; X = CH2, CH2CH2, CH2O; Y = CH2, CH2CH2, CH2O; Z = (substituted) 1,2-arylene, 1,2-heteroarylene; R1, R2 = H, cyano, alkyl, aryl, aralkyl, heteroaralkyl, alkenyl, etc.; R3, R4 = H, halo, CF3, cyano, alkyl, alkoxy; with provisos], were prepared Thus, 6-amino-5,6,7,8-tetrahydroquinoline, 5-chloroindole-2-carboxylic acid, 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride, and 1-hydroxy-7-azabenzotriazole were stirred 2 h in THF to give 43% 5-chloroindole-2-carboxylic acid (5,6,7,8-tetrahydroquinolin-6-yl)amide. I deemed to posess activity as

L11 ANSWER 13 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
glycogen phosphorylase inhibitors demonstrate IC50 ≤10 μM.
IT 887761-56-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of chloroindolecarboxamides as glycogen phosphorylase inhibitors)
RN 887761-56-0 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(3R)-3-[[(cyanomethyl)methylamino]carbonyl]-1,2,3,4-tetrahydro-2-naphthalenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



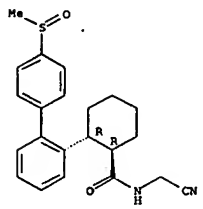
L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:47977 CAPLUS
DOCUMENT NUMBER: 144:184036
TITLE: β-Substituted Cyclohexanecarboxamide: A Nonpeptidic Framework for the Design of Potent Inhibitors of Cathepsin K
AUTHOR(S): Crane, Sheldon N.; Black, W. Cameron; Palmer, James T.; Davis, Dana E.; Setti, Eduardo; Robichaud, Joel; Paquet, Julie; Oballa, Renata M.; Bayly, Christopher I.; McKay, Daniel J.; Somoza, John R.; Chauret, Natalie; Seto, Carmai; Scheigetz, John; Wesolowski, Greg; Masse, Frederic; Desmarais, Sylvie; Ouellet, Marc
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Kirkland, QC, H9H 3L1, Can.
SOURCE: Journal of Medicinal Chemistry (2006), 49(3), 1066-1079
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:184036
GI



I

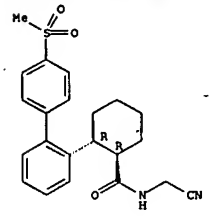
AB A new series of nonpeptidic cathepsin K inhibitors that are based on a β-substituted cyclohexanecarboxamide motif has been developed. Lead optimization yielded compds. with sub-nanomolar potency and exceptional selectivity profiles against cathepsins B, L, and S. Use of fluorine atoms to block metabolism on the cyclohexyl ring led to compds. with excellent pharmacokinetic properties. Considering the well-established role of cathepsin K in osteoclast-mediated bone turnover, compds. such as I (hrab Cat K IC50 0.28 nM; >800-fold selectivity vs Cat B, L, and S; PK data in dogs: F 55%, t1/2 = 15 h) exhibit great potential for development as an orally bioavailable therapeutic for treatment of diseases that involve bone loss.
IT 530106-95-7 875142-68-0 875142-70-4

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 875142-74-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(methylsulfonyl)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

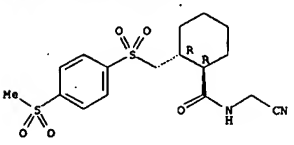


IT 530104-82-6P 819858-00-9P 819858-02-1P
875142-62-4P 875142-64-6P 875142-66-8P
875142-76-0P 875142-78-2P 875142-81-7P
875142-83-9P 875142-86-2P 875142-88-4P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β-substituted cyclohexanecarboxamides as cathepsin K inhibitors)
RN 530104-82-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(methylthio)phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

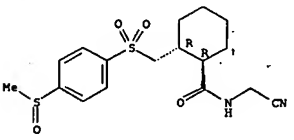
L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
875142-74-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-substituted cyclohexanecarboxamides as cathepsin K inhibitors)
RN 530106-95-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(methylsulfonyl)phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 875142-68-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(methylsulfinyl)phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

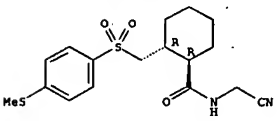
Relative stereochemistry.



RN 875142-70-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(methylsulfinyl)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

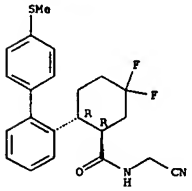
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



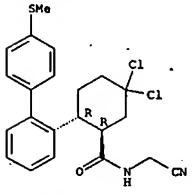
RN 819858-00-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 819858-02-1 CAPLUS
CN Cyclohexanecarboxamide, 5,5-dichloro-N-(cyanomethyl)-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

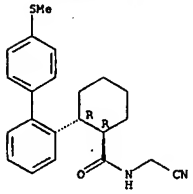
Relative stereochemistry.



RN 875142-62-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

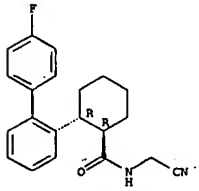
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



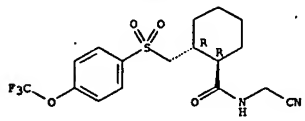
RN 875142-64-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-fluoro[1,1'-biphenyl]-2-yl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 875142-66-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(trifluoromethoxy)phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

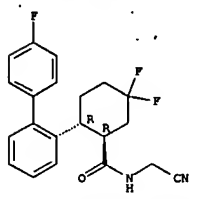


RN 875142-76-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(trifluoromethoxy)phenyl-2-

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

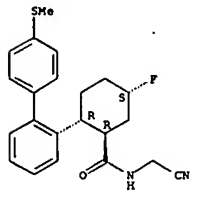
RN 875142-83-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-(4'-fluoro[1,1'-biphenyl]-2-yl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 875142-86-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5-fluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

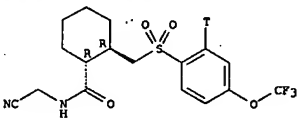


RN 875142-88-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5-fluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

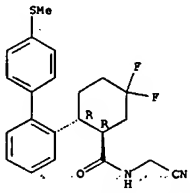
L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
t]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



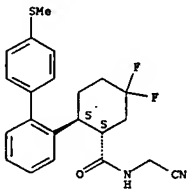
RN 875142-78-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (CA INDEX NAME)

Relative stereochemistry.

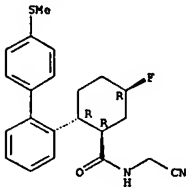


RN 875142-81-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1S,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

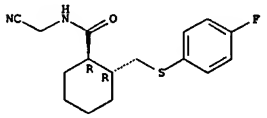


L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 530104-11-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(β-substituted cyclohexanecarboxamides as cathepsin K inhibitors)
RN 530104-11-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-fluorophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 530104-17-7P 530104-19-9P 530104-21-3P
530104-25-7P 530104-27-9P 530104-86-0P
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530108-65-7P 530108-67-9P 530108-69-1P
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875142-39-5P 875142-42-0P 875142-45-3P
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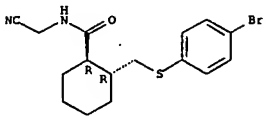
875142-58-8P 875142-60-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β-substituted cyclohexanecarboxamides as cathepsin K inhibitors)
RN 530104-17-7 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(4-bromophenyl)thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

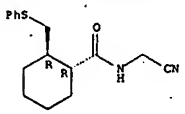
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



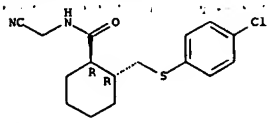
RN 530104-19-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(phenylthio)methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-21-3 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(4-chlorophenyl)thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

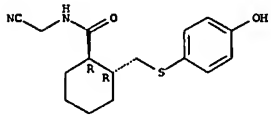
Relative stereochemistry.



RN 530104-25-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-methylphenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

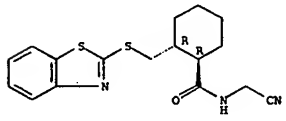
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



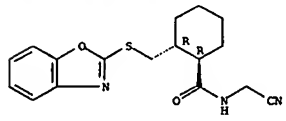
RN 530107-01-8 CAPLUS
CN Cyclohexanecarboxamide, 2-[(2-benzothiazolylthio)methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



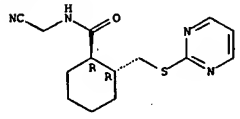
RN 530107-03-0 CAPLUS
CN Cyclohexanecarboxamide, 2-[(2-benzoxazolylthio)methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



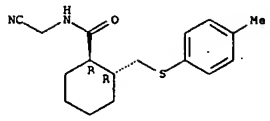
RN 530107-09-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(2-pyrimidinylthio)methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



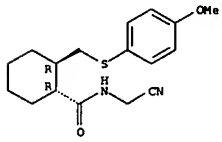
Karen Cheng

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



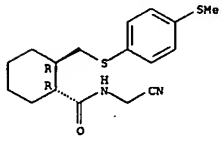
RN 530104-27-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-methoxyphenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-86-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(methylthio)phenyl]thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



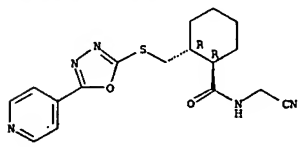
RN 530104-88-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-hydroxyphenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

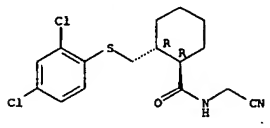
RN 530107-24-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[5-(4-pyridinyl)-1,3,4-oxadiazol-2-yl]thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



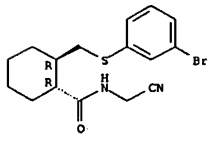
RN 530107-30-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(2,4-dichlorophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530108-65-7 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(3-bromophenyl)thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

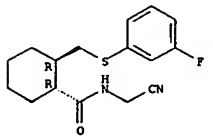
Relative stereochemistry.



RN 530108-67-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(3-fluorophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

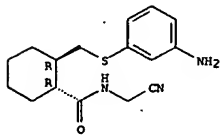
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



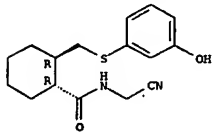
RN 530108-69-1 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(3-aminophenyl)thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530108-76-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(3-hydroxyphenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

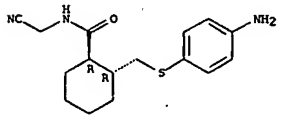
Relative stereochemistry.



RN 530109-04-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-iodophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

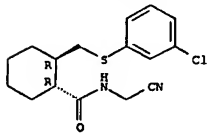
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



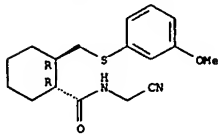
RN 875142-35-1 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(3-chlorophenyl)thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 875142-39-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(3-methoxyphenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

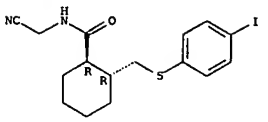
Relative stereochemistry.



RN 875142-42-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(3,5-dichlorophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

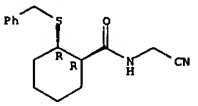
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



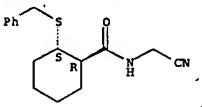
RN 875142-15-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(phenylmethyl)thio]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 875142-17-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(phenylmethyl)thio]-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

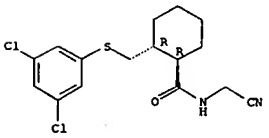
Relative stereochemistry.



RN 875142-32-8 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(4-aminophenyl)thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

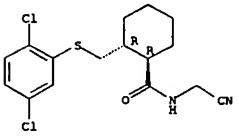
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



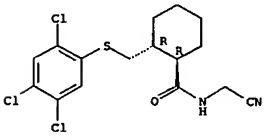
RN 875142-45-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(2,5-dichlorophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 875142-47-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(2,4,5-trichlorophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

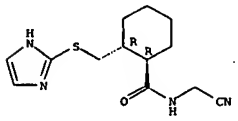
Relative stereochemistry.



RN 875142-49-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(1H-imidazol-2-ylthio)methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

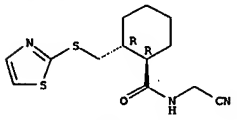
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



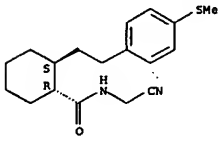
RN 875142-54-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(2-thiazolylthio)methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 875142-58-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2-[4-(methylthio)phenyl]ethyl]-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

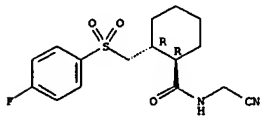


RN 875142-60-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(1Z)-2-[4-(methylthio)phenyl]ethenyl]-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

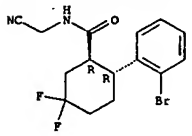
L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Relative stereochemistry.



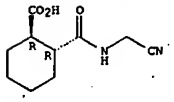
RN 819858-51-0 CAPLUS
CN Cyclohexanecarboxamide, 2-(2-bromophenyl)-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



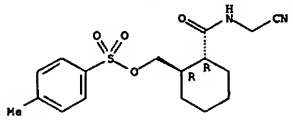
RN 875142-92-0 CAPLUS
CN Cyclohexanecarboxylic acid, 2-[[(cyanomethyl)amino]carbonyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



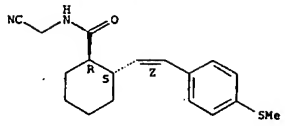
RN 875142-94-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[(4-methylphenyl)sulfonyl]oxy]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



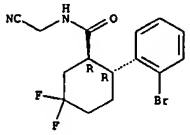
Karen Cheng

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



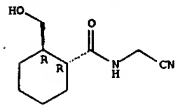
IT 926312-34-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(β-substituted cyclohexanecarboxamides as cathepsin K inhibitors)
RN 926312-34-7 CAPLUS
CN Cyclohexanecarboxamide, 2-(2-bromophenyl)-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)-rel- (CA INDEX NAME)

Relative stereochemistry.



IT 530104-13-3P 530104-43-9P 819858-51-0P
875142-92-0P 875142-94-2P 875143-32-1P
875143-37-6P 875143-39-8P 875143-69-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(β-substituted cyclohexanecarboxamides as cathepsin K inhibitors)
RN 530104-13-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(hydroxymethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

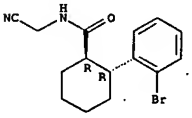


RN 530104-43-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-fluorophenyl)sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

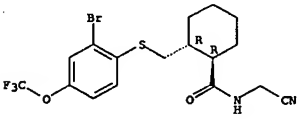
RN 875143-32-1 CAPLUS
CN Cyclohexanecarboxamide, 2-(2-bromophenyl)-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



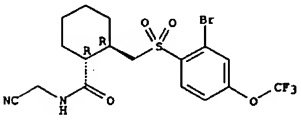
RN 875143-37-6 CAPLUS
CN Cyclohexanecarboxamide, 2-[[[2-bromo-4-(trifluoromethoxy)phenyl]thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 875143-39-8 CAPLUS
CN Cyclohexanecarboxamide, 2-[[[2-bromo-4-(trifluoromethoxy)phenyl]sulfonyl]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

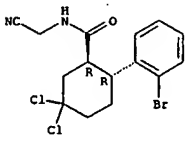
Relative stereochemistry.



RN 875143-69-4 CAPLUS
CN Cyclohexanecarboxamide, 2-(2-bromophenyl)-5,5-dichloro-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

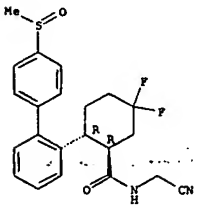
Relative stereochemistry.

L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 926311-55-9P 926311-58-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(β-substituted cyclohexanecarboxamides as cathepsin K inhibitors)
RN 926311-55-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-(methylsulfinyl)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (CA INDEX NAME)

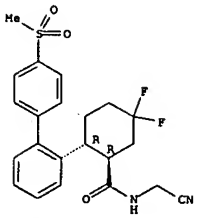
Relative stereochemistry.



RN 926311-58-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-(methylsulfonyl)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (CA INDEX NAME)

Relative stereochemistry.

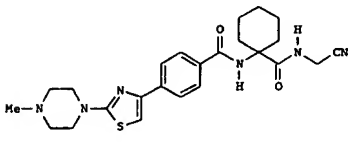
L11 ANSWER 14 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

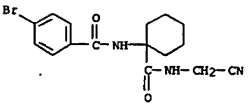
ACCESSION NUMBER: 2005:1163295 CAPLUS
DOCUMENT NUMBER: 144:69602
TITLE: Design and synthesis of tri-ring P3 benzamide-containing aminonitriles as potent, selective, orally effective inhibitors of cathepsin K
AUTHOR(S): Palmer, James T.; Bryant, Clifford; Wang, Dan-Xiong; Davis, Dana E.; Setti, Eduardo L.; Rydzewski, Robert M.; Venkatraman, Shankar; Tian, Zong-Qiang; Burrill, Leland C.; Mendonca, Rohan V.; Springman, Eric; McCarter, John; Chung, Tobee; Cheung, Harry; Janc, James W.; McGrath, Mary; Somoza, John R.; Enriquez, Philip; Yu, Z. Walter; Strickley, Robert M.; Liu, Liang; Venuti, Michael C.; Percival, M. David; Falgueyret, Jean-Pierre; Prasit, Peppi; Oballa, Renata; Riendeau, Denis; Young, Robert N.; Wesolowski, Gregg; Rodan, Sevgi B.; Johnson, Colena; Kimmel, Donald B.; Rodan, Gideon
CORPORATE SOURCE: Celera Genomics, Inc., South San Francisco, CA, 94080, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(24), 7520-7534
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:69602
GI



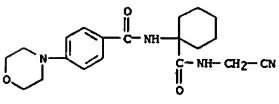
I

AB A series of achiral aminoacetonitriles, bearing tri-ring benzamide moieties and an aminocyclohexanecarboxylate residue was prepared This combination of binding elements resulted in sub-250 pM, reversible, selective, and orally bioavailable cathepsin K inhibitors. Lead compds. displayed single digit nanomolar inhibition in vitro (of rabbit osteoclast-mediated degradation of bovine bone). The best compound in this series, I (CRA-013783/L-006235), was orally bioavailable in rats, with a terminal half-life of over 3 h. I was dosed orally in ovariectomized rhesus monkeys once per day for 7 days. Collagen breakdown products were reduced by up to 76% dose-dependently. Plasma concns. of I above the bone resorption IC50 after 24 h indicated a correlation between functional cellular and in vivo assays. Inhibition of collagen breakdown by cathepsin K inhibitors suggests this mechanism of action may be useful in osteoporosis and other indications involving bone resorption.
IT 871828-07-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cathepsin inhibitory activity of [(arylamido)cyclohexyl]carbonylaminoacetonitriles starting from (Boc-amino)cyclohexanecarboxylic acid using a multistep procedure)
RN 871828-07-8 CAPLUS
CN Benzamide, 4-bromo-N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

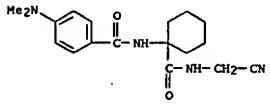


IT 294622-31-4P 294622-33-6P 294622-34-7P
294622-35-8P 294622-36-9P 294622-37-0P
294622-81-4P 294623-49-7P 354813-19-7P
871828-05-6P 871828-06-7P 871828-08-9P
871828-09-0P 871828-10-3P 871828-11-4P
871828-12-5P 871828-13-6P 871828-17-0P
871828-24-9P 871828-25-0P 871828-37-4P
871828-38-5P 871828-39-6P 871828-40-9P
871828-41-0P 871828-42-1P 871828-43-2P
871828-44-3P 871828-45-4P 871828-46-5P
871828-47-6P 871828-48-7P 871828-63-6P
871828-64-7P 871828-65-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and cathepsin inhibitory activity of [(arylamido)cyclohexyl]carbonylaminoacetonitriles starting from (Boc-amino)cyclohexanecarboxylic acid using a multistep procedure)
RN 294622-31-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

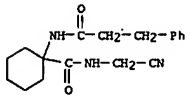


RN 294622-33-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

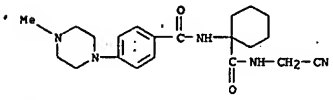
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



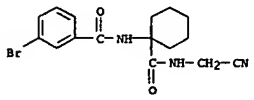
RN 294622-34-7 CAPLUS
CN Benzenepropanamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)



RN 294622-35-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

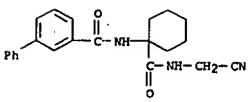


RN 294622-36-9 CAPLUS
CN Benzamide, 3-bromo-N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

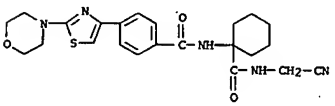


RN 294622-37-0 CAPLUS
CN [1,1'-Biphenyl]-3-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

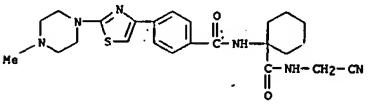
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



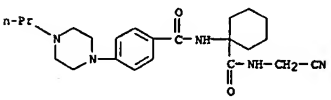
RN 294622-81-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 294623-49-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

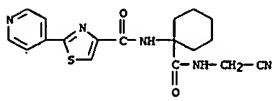


RN 354813-19-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)

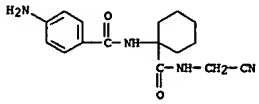


RN 871828-05-6 CAPLUS
CN 4-Thiazolecarboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-2-(4-

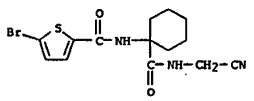
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
pyridinyl)- (9CI) (CA INDEX NAME)



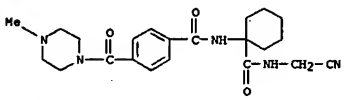
RN 871828-06-7 CAPLUS
CN Benzamide, 4-amino-N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)



RN 871828-08-9 CAPLUS
CN 2-Thiophenecarboxamide, 5-bromo-N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

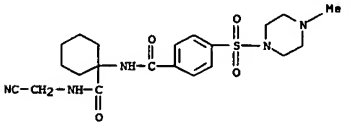


RN 871828-09-0 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[(4-methyl-1-piperazinyl)carbonyl]- (9CI) (CA INDEX NAME)

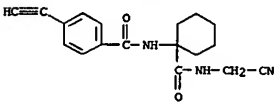


RN 871828-10-3 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[(4-methyl-1-piperazinyl)sulfonyl]- (9CI) (CA INDEX NAME)

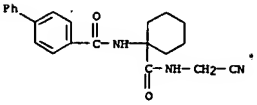
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



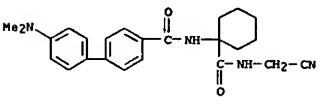
RN 871828-11-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-ethynyl- (9CI) (CA INDEX NAME)



RN 871828-12-5 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)



RN 871828-13-6 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4'-(dimethylamino)- (9CI) (CA INDEX NAME)



RN 871828-17-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4'-[methyl(1-methyl-3-pyrrolidinyl)amino]- (9CI) (CA INDEX NAME)

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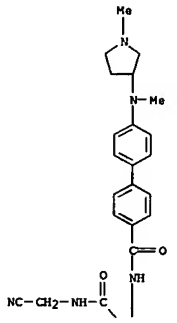

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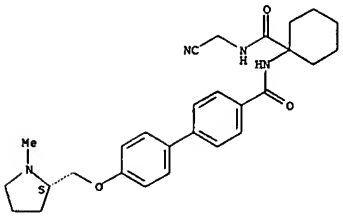
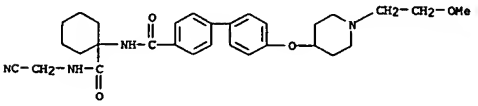
RN 871828-24-9 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-[[(2S)-1-methyl-2-pyrrolidinyl]methoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

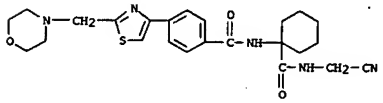
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 871828-25-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-[[1-(2-methoxyethyl)-4-piperidinyl]oxy]- (9CI) (CA INDEX NAME)

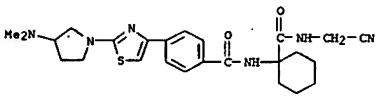


RN 871828-37-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinylmethyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

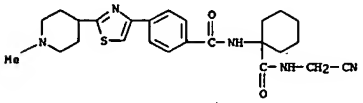


RN 871828-38-5 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-[3-(dimethylamino)-1-pyrrolidinyl]-4-thiazolyl]- (9CI) (CA INDEX NAME)

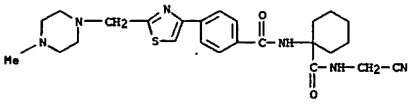
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 871828-39-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(1-methyl-4-piperidinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

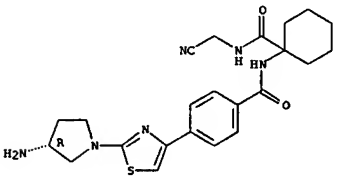


RN 871828-40-9 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-[(4-methyl-1-piperazinyl)methyl]-4-thiazolyl]- (9CI) (CA INDEX NAME)



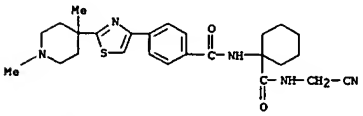
RN 871828-41-0 CAPLUS
CN Benzamide, 4-[2-[(3R)-3-amino-1-pyrrolidinyl]-4-thiazolyl]-N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

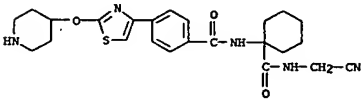


RN 871828-42-1 CAPLUS

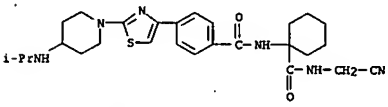
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(1,4-dimethyl-4-piperidinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



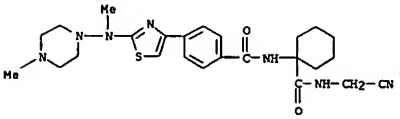
RN 871828-43-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-piperidinyloxy)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 871828-44-3 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-[4-[(1-methylethyl)amino]-1-piperidinyl]-4-thiazolyl]- (9CI) (CA INDEX NAME)

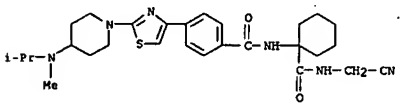


RN 871828-45-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-[methyl(4-methyl-1-piperazinyl)amino]-4-thiazolyl]- (9CI) (CA INDEX NAME)

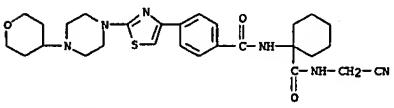


RN 871828-46-5 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-[4-

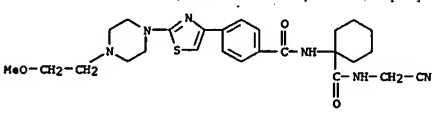
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
[methyl(1-methylethyl)amino]-1-piperidinyl]-4-thiazolyl]- (9CI) (CA INDEX NAME)



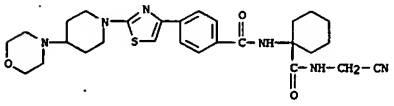
RN 871828-47-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-[4-(tetrahydro-2H-pyran-4-yl)-1-piperazinyl]-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 871828-48-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-[4-(2-methoxyethyl)-1-piperazinyl]-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 871828-63-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-[4-(4-morpholinyl)-1-piperidinyl]-4-thiazolyl]- (9CI) (CA INDEX NAME)



L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

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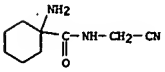
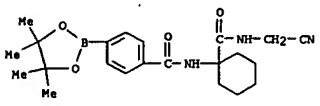
CMF C9 H15 N3 O



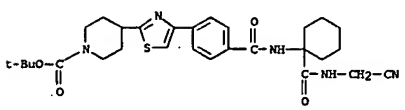
CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 871828-15-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)- (9CI) (CA INDEX NAME)



RN 871828-55-6 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

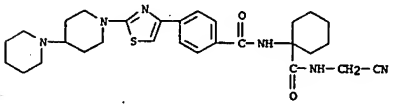


RN 871828-57-8 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

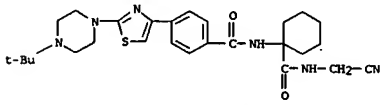
Karen Cheng

L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 871828-64-7 CAPLUS
CN Benzamide, 4-(2-[1,4'-bipiperidin]-1'-yl-4-thiazolyl)-N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

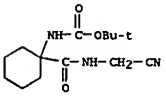


RN 871828-65-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-[4-(1,1-dimethylethyl)-1-piperazinyl]-4-thiazolyl]- (9CI) (CA INDEX NAME)



IT 225122-33-8P 294622-49-4P 871828-15-8P
871828-55-6P 871828-57-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cathepsin inhibitory activity of [(arylamido)cyclohexyl]carbonylaminoacetonitriles starting from (Boc-amino)cyclohexanecarboxylic acid using a multistep procedure)

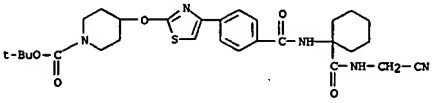
RN 225122-33-8 CAPLUS
CN Carbamic acid, [1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 294622-49-4 CAPLUS
CN Cyclohexanecarboxamide, 1-amino-N-(cyanomethyl)-, monomethanesulfonate (9CI) (CA INDEX NAME)

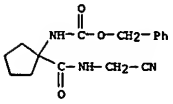
CM 1

L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

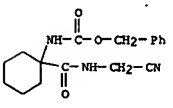


IT 871828-00-1P 871828-01-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and cathepsin inhibitocy activity of aminoacetonitrile derivs.
via amidation of N-Cbz-amino acids)

RN 871828-00-1 CAPLUS
CN Carbamic acid, [1-[[(cyanomethyl)amino]carbonyl]cyclopentyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



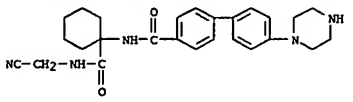
RN 871828-01-2 CAPLUS
CN Carbamic acid, [1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



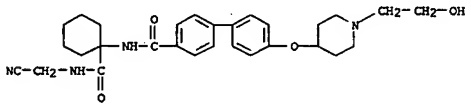
IT 867011-65-2P 871828-16-9P 871828-18-1P
871828-19-2P 871828-20-5P 871828-21-6P
871828-22-7P 871828-23-8P 871828-26-1P
871828-27-2P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, cathepsin inhibitory activity, and pharmacokinetics of [(arylamido)cyclohexyl]carbonylaminoacetonitriles starting from (Boc-amino)cyclohexanecarboxylic acid using a multistep procedure)

RN 867011-65-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4'-(1-piperazinyl)- (9CI) (CA INDEX NAME)

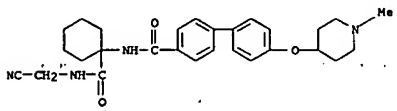
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



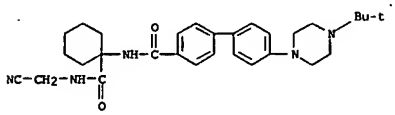
RN 871828-16-9 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-[[1-(2-hydroxyethyl)-4-piperidinyl]oxy]- (9CI) (CA INDEX NAME)



RN 871828-18-1 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-[(1-methyl-4-piperidinyl)oxy]- (9CI) (CA INDEX NAME)

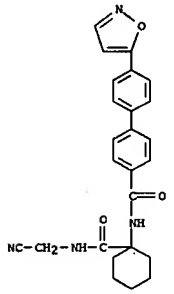


RN 871828-19-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-[4-(1,1-dimethylethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

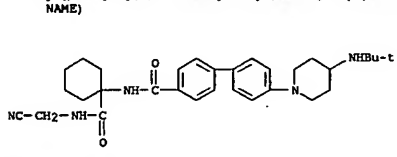


RN 871828-20-5 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-(1-piperazinylsulfonyl)- (9CI) (CA INDEX NAME)

L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
yl]-4'-(5-isoxazolyl)- (9CI) (CA INDEX NAME)

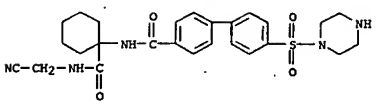


RN 871828-27-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-[4-[(1,1-dimethylethyl)amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

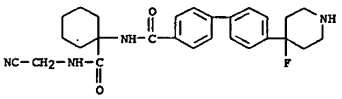


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

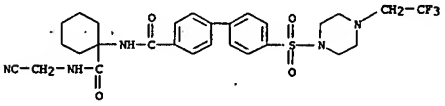
L11 ANSWER 15 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



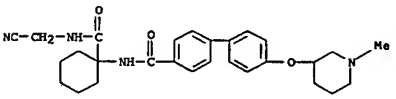
RN 871828-21-6 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-(4-fluoro-4-piperidinyl)- (9CI) (CA INDEX NAME)



RN 871828-22-7 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-[[4-(2,2,2-trifluoroethyl)-1-piperazinyl]sulfonyl]- (9CI) (CA INDEX NAME)



RN 871828-23-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex yl]-4'-[(1-methyl-3-piperidinyl)oxy]- (9CI) (CA INDEX NAME)



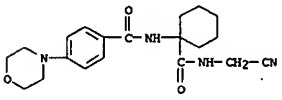
RN 871828-26-1 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohex

L11 ANSWER 16 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1163288 CAPLUS
DOCUMENT NUMBER: 144:546
TITLE: Lysosomotropism of Basic Cathepsin K Inhibitors Contributes to Increased Cellular Potencies against Off-Target Cathepsins and Reduced Functional Selectivity
AUTHOR(S): Falgueyret, Jean-Pierre; Desmarais, Sylvie; Oballa, Renata; Black, W. Cameron; Cromlish, Wanda; Khougaz, Karine; Lamontagne, Sonia; Masse, Frederic; Riendeau, Denis; Toulmond, Sylvie; Percival, M. David
CORPORATE SOURCE: Departments of Biochemistry, Molecular Biology and Pharmacology, Medicinal Chemistry, and Pharmaceutical Research and Development, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, Can.
SOURCE: Journal of Medicinal Chemistry (2005), 48(24), 7535-7543
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:546

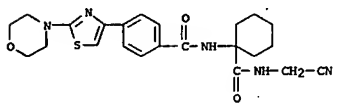
AB The lysosomal cysteine protease cathepsin K is a target for osteoporosis therapy. The aryl-piperazine-containing cathepsin K inhibitor CRA-013783/L-006235 (1) displays greater than 4000-fold selectivity against the lysosomal/endosomal antitargets cathepsin B, L, and S. However, 1 and other aryl-piperazine-containing analogs, including balicatib (10), are .apprx.10-100-fold more potent in cell-based enzyme occupancy assays than against each purified enzyme. This phenomenon arises from their basic, lipophilic nature, which results in lysosomal trapping. Consistent with its lysosomotropic nature, 1 accumulates in cells and in rat tissues of high lysosome content. In contrast, nonbasic aryl-morpholino-containing analogs do not exhibit lysosomotropic properties. Increased off-target activities of basic cathepsin K inhibitors were observed in a cell-based cathepsin S antigen presentation assay. No potency increases of basic inhibitors in a functional cathepsin K bone resorption whole cell assay were detected. Therefore, basic cathepsin K inhibitors, such as 1, suffer from reduced functional selectivities compared to those predicted using purified enzyme assays.

IT 294622-31-4 294622-81-4 294623-49-7, L 006235
354813-19-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(piperazine and morpholino-containing cathepsin K inhibitors preparation, lysosomotropic and cathepsins B,K,L, and S inhibiting properties)

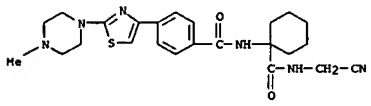
RN 294622-31-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)



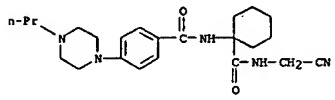
L11 ANSWER 16 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 294622-81-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 294623-49-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)



RN 354813-19-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)

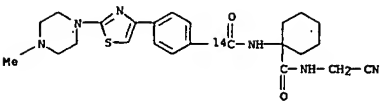


IT 870100-92-8P
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(piperazine and morpholino-containing cathepsin K inhibitors preparation, lysosomotropic and cathepsins B,K,L, and S inhibiting properties)
RN 870100-92-8 CAPLUS
CN Formic acid, compd. with N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]benzamide-carbonyl-14C (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 870100-91-7

L11 ANSWER 16 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CMF C24 H30 N6 O2 S

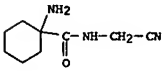


CM 2

CRN 64-18-6
CMF C H2 O2

O=CH-OH

IT 225122-32-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(piperazine and morpholino-containing cathepsin K inhibitors preparation, lysosomotropic and cathepsins B,K,L, and S inhibiting properties)
RN 225122-32-7 CAPLUS
CN Cyclohexanecarboxamide, 1-amino-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

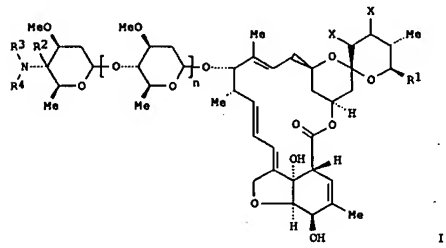


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 17 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1130654 CAPLUS
DOCUMENT NUMBER: 143:406091
TITLE: Preparation of avermectin and avermectin monosaccharide substituted in the 4"- and 4'-position respectively as parasiticides
INVENTOR(S): Jung, Pierre Joseph Marcel; Paterna, Thomas; Quaranta, Laura; Hueter, Ottmar Franz; Murphy-Kessabi, Fiona Mary
PATENT ASSIGNEE(S): Syngenta Participations A.-G., Switz.
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005097816	A1	20051020	WO 2005-EP2489	20050309
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1737876	A1	20070103	EP 2005-715877	20050309
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: EP 2004-8413 A 20040407
WO 2005-EP2489 W 20050309
OTHER SOURCE(S): CASREACT 143:406091; MARPAT 143:406091
GI



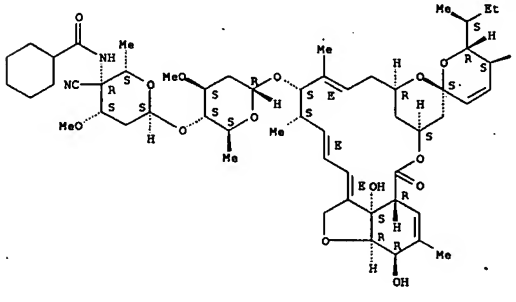
I

L11 ANSWER 17 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB Title avermectin derivs. I were prepared, wherein X = H, XX is a bond; n is 0 or 1, R1 represents a alkyl, cycloalkyl, alkenyl, R2 represents hydrocarbyl, R3 and R4 represent, independently of each other, hydrogen or a chemical constituent, or either R2 and R3 together or R3 and R4 together represent a three- to seven-membered alkylene or a four- to seven-membered alkenylene bridge, for each of which at least one, preferably a CH2 group may be replaced by O, S or NR where R represents hydrogen or a hydrocarbyl group; or if appropriate, an E/Z isomer and/or tautomer of the compound of formula I, in each case in free form or in salt form. Thus, I (XX is a bond, n = 1, R1 = sec-Bu, R2 = Me, R3 = R4 = H) was prepared as parasiticides. An especially important aspect of the present invention is the use of title compds. of in the protection of plants against parasitic feeding pests. The action of I and the compns. comprising the said compound against animal pests can be significantly broadened and adapted to the given circumstances by the addition of other insecticides, acaricides or nematicides.
IT 867051-09-0P 867051-10-3P
RL: BSU (Biological study, unclassified); IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of avermectin and avermectin monosaccharide substituted in the 4"- and 4'-position resp. as parasiticides)
RN 867051-09-0 CAPLUS
CN Avermectin Ala, 4''-cyano-4''-[(cyclohexylcarbonyl)amino]-5-O-demethyl-4''-deoxy-, (4''R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



Karen Cheng

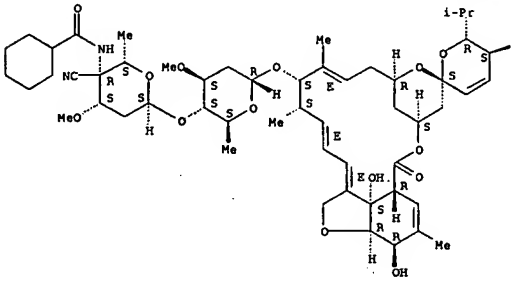
L11 ANSWER 17 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-B

RN 867051-10-3 CAPLUS
CN Avermectin A1a, 4''-cyano-4''-[(cyclohexylcarbonyl)amino]-5-O-demethyl-25-de(1-methylpropyl)-4''-deoxy-25-(1-methylethyl)-, (4''R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

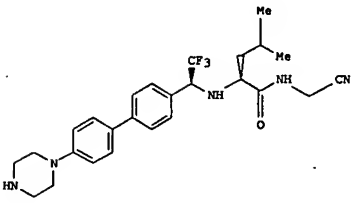


PAGE 1-B

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

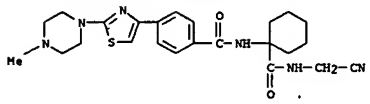
ACCESSION NUMBER: 2005:1024918 CAPLUS
DOCUMENT NUMBER: 143:398880
TITLE: Trifluoroethylamines as amide isosteres in inhibitors of cathepsin K
AUTHOR(S): Black, W. Cameron; Bayly, Christopher I.; Davis, Dana E.; Desmarais, Sylvie; Falgueyret, Jean-Pierre; Leger, Serge; Li, Chun Sing; Masse, Frederic; McKay, Daniel J.; Palmer, James T.; Percival, M. David; Robichaud, Joel; Tsou, Nancy; Zamboni, Robert
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Pointe-Claire-Dorval, QC, H9R 4P8, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(21), 4741-4744
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:398880
GI



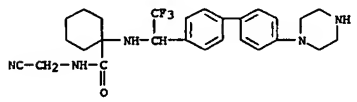
I

AB The P2-P3 amide of dipeptide cathepsin K inhibitors can be replaced by the metabolically stable trifluoroethylamine group. The nonbasic nature of the nitrogen allows the important hydrogen bond to Gly66 to be made. The resulting compds. are 10- to 20-fold more potent than the corresponding amide derivs. Compound (I) is a 5 pM inhibitor of human cathepsin K with >10,000-fold selectivity over other cathepsins.
IT 294623-49-7, L-006235 603140-33-6 867011-65-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trifluoroethylamines as amide isosteres in inhibitors of cathepsin K)
RN 294623-49-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

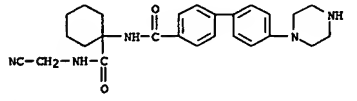
L11 ANSWER 18 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 603140-33-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[[2,2,2-trifluoro-1-[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]- (9CI) (CA INDEX NAME)



RN 867011-65-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4'-(1-piperazinyl)- (9CI) (CA INDEX NAME)

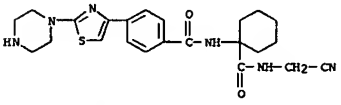


REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

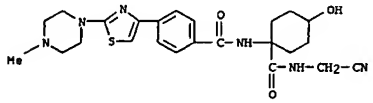
ACCESSION NUMBER: 2005:674881 CAPLUS
DOCUMENT NUMBER: 143:298359
TITLE: A strategy for identification of drug metabolites from dried blood spots using triple-quadrupole/linear ion trap hybrid mass spectrometry
AUTHOR(S): Mauriala, Timo; Chauret, Nathalie; Oballa, Renata; Nicoll-Griffith, Deborah A.; Bateman, Kevin P.
CORPORATE SOURCE: Merck Frosst Canada Inc., Kirkland, QC, H9H 3L1, Can.
SOURCE: Rapid Communications in Mass Spectrometry (2005), 19(14), 1984-1992
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Discovery stage studies that address issues of absorption, distribution, metabolism and excretion (ADME) are vital for lead optimization resulting in new drug candidates. Often pharmacokinetics (PK) is assessed in these expts. without regard for the metabolism of the compound or the potential for metabolites to circulate in vivo. This work presents a strategy for drug level determination and detection of metabolites using dried blood spots for sample collection. Initially, metabolites are detected from microsomal incubations and characterized using tandem mass spectrometry. Data dependent enhanced MS and enhanced product ion (EMS-EPI) scanning with dynamic background subtraction was used on a hybrid quadruple linear ion trap mass spectrometer. On-the-fly background subtraction greatly improved the detection of metabolites. These data were used to build a multiple reaction monitoring (MRM) method for the parent and metabolites. MRM-EPI scanning was used to analyze the extracted dried blood spots from the PK study. Circulating metabolites were detected using MRM and their identities confirmed on the basis of fragment ion spectra collected simultaneously. The use of dried blood spots provides a means for re-anal. of PK samples for metabolite identification without the need for complex sample storage and preparation Both parent compound and metabolite information can be collected in these studies, resulting in a savings of time and resources.
IT 294623-09-9 864957-87-9 864957-89-1 864957-94-8
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(strategy for identification of drug metabolites from dried blood spots using triple-quadrupole/linear ion trap hybrid mass spectrometry)
RN 294623-09-9 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(1-piperazinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

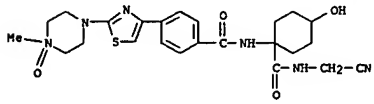


RN 864957-87-9 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]-4-hydroxycyclohexyl]-4-[2-

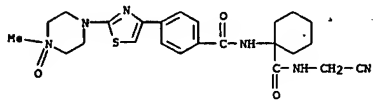
L11 ANSWER 19 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(4-methyl-1-piperazinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 864957-89-1 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]-4-hydroxycyclohexyl]-4-[2-(4-methyl-4-oxido-1-piperazinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

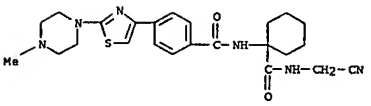


RN 864957-94-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-4-oxido-1-piperazinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



IT 294623-49-7, L 006235
RL: ANT (Analyte); PKT (Pharmacokinetics); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(strategy for identification of drug metabolites from dried blood spots using triple-quadrupole/linear ion trap hybrid mass spectrometry)
RN 294623-49-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

L11 ANSWER 19 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



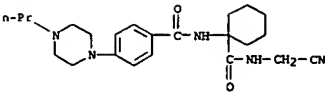
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:471953 CAPLUS
DOCUMENT NUMBER: 143:1333
TITLE: Use of cathepsin K inhibitors in severe bone loss diseases
INVENTOR(S): Missbach, Martin; Gamse, Rainer; Trechsel, Ulrich
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049028	A1	20050602	WO 2004-EP4155	20040419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004290874	A1	20050602	AU 2004-290874	20040419
CA 2545723	A1	20050602	CA 2004-2545723	20040419
EP 1686995	A1	20060809	EP 2004-728182	20040419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1882343	A	20061220	CN 2004-80033754	20040419
BR 2004016755	A	20070227	BR 2004-16755	20040419
JP 2007511548	T	20070510	JP 2006-540184	20040419
US 2007135448	A1	20070614	US 2006-578167	20060504
NO 2006002870	A	20060818	NO 2006-2870	20060619
PRIORITY APPLN. INFO.:			EP 2003-26430 A	20031119
			WO 2004-EP4155 W	20040419

OTHER SOURCE(S): MARPAT 143:1333
AB The invention relates generally to cathepsin K inhibitors and their use in bone growth. Specifically, the invention relates to the use of cathepsin K inhibitors to stimulate new bone formation in patients in need thereof. Compds. of the invention include e.g. N-[1-(cyanomethylcarbamoyl)cyclohexyl]-4-(4-propylpiperazin-1-yl)benzamide.
IT 354813-19-7 843609-18-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cathepsin K inhibitors for severe bone loss diseases)
RN 354813-19-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)

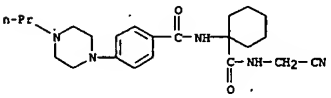
L11 ANSWER 20 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 843609-18-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 354813-19-7
CMF C23 H33 N5 O2



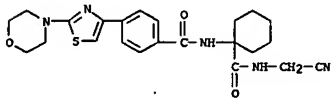
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:331984 CAPLUS
DOCUMENT NUMBER: 143:381598
TITLE: An activity-based probe for the determination of cysteine cathepsin protease activities in whole cells. [Erratum to document cited in CA142:129533]
AUTHOR(S): Falgueyret, Jean-Pierre; Black, W. Cameron; Cromlish, Wanda; Desmarais, Sylvie; Lamontagne, Sonia; Mellon, Christophe; Riendeau, Denis; Rodan, Sevgi B.; Tawa, Paul; Wesolowski, Gregg; Bass, Kathryn E.; Venkatraman, Shankar; Percival, M. David
CORPORATE SOURCE: Departments of Biochemistry and Molecular Biology and Medicinal Chemistry, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, Can.
SOURCE: Analytical Biochemistry (2005), 340(2), 380
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sevgi B. Rodan and Gregg Wesolowski are affiliated with Merck Research Laboratories, West Point, PA, USA, which should have been listed as the "b" affiliation. Kathryn E. Bass and Shankar Venkatraman are affiliated with Celera, South San Francisco, CA, USA, which should have been denoted by a "c". The correct author and affiliation lines are given.
IT 294622-81-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; diazomethylketone-containing irreversible inhibitor preparation as
activity-based probe for determination of cathepsin in whole cells (Erratum))
RN 294622-81-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

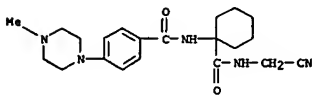


L11 ANSWER 22 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:136573 CAPLUS
DOCUMENT NUMBER: 142:212408
TITLE: Combinations of a cathepsin K inhibitor and a bisphosphonate in the treatment of bone metastasis, tumor growth, tumor-induced bone loss, and bone loss diseases
INVENTOR(S): Zimmermann, Johann; Goessl, Carsten
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

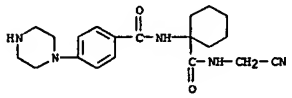
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014006	A1	20050217	WO 2004-EP8107	20040720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004262903	A1	20050217	AU 2004-262903	20040720
CA 2532948	A1	20050217	CA 2004-2532948	20040720
EP 1651238	A1	20060503	EP 2004-741174	20040720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1826124	A	20060830	CN 2004-80021110	20040720
BR 2004012769	A	20060926	BR 2004-12769	20040720
JP 2006528151	T	20061214	JP 2006-520778	20040720
IN 2006CN00226	A	20070629	IN 2006-CN226	20060118
NO 2006000851	A	20060421	NO 2006-851	20060221
US 2006281714	A1	20061214	US 2006-565453	20060518

PRIORITY APPLN. INFO.: US 2003-488925P P 20030721
WO 2004-EP8107 W 20040720
OTHER SOURCE(S): MARPAT 142:212408
AB The invention discloses pharmaceutical prepns. comprising certain types of bisphosphonates and certain types of Cathepsin K inhibitors, in particular for the prevention and treatment of bone metastases, tumor-induced hypercalcemia, tumor growth, tumor-induced bone loss and bone loss diseases such as osteoporosis or cancer therapy-induced bone loss.
IT 294622-35-8 354813-10-8 354813-16-4
354813-19-7 354813-22-2 354813-25-5
354813-28-8 354813-31-3 354813-34-6
354813-39-1 354813-43-7 354813-47-1
354813-50-6 843609-17-6 843609-18-7
843609-19-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

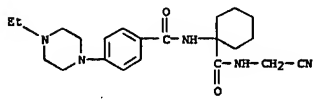
L11 ANSWER 22 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(Biological study); USES (Uses)
(cathepsin K inhibitor-bisphosphonate combination for treatment of bone metastasis, tumor growth, tumor-induced bone loss, and bone loss diseases)
RN 294622-35-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



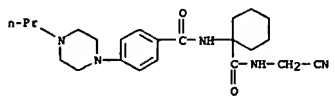
RN 354813-10-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 354813-16-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-ethyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



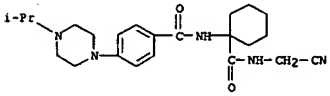
RN 354813-19-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)



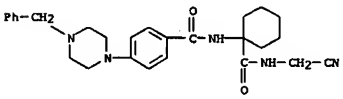
Karen Cheng

L11 ANSWER 22 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

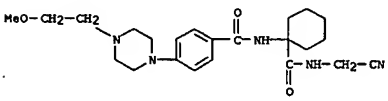
RN 354813-22-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[4-(1-methylethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



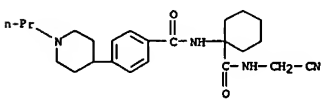
RN 354813-25-5 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[4-(phenylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 354813-28-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[4-(2-methoxyethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 354813-31-3 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-propyl-4-piperidinyl)- (9CI) (CA INDEX NAME)



RN 354813-34-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[1-(2-

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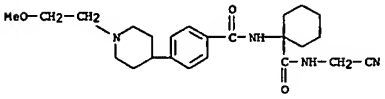
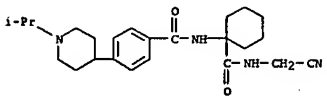
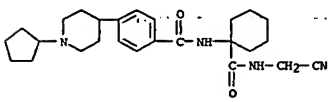
methoxyethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



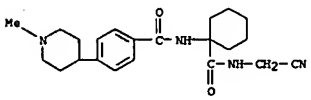
RN 354813-39-1 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 354813-43-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-cyclopentyl-4-piperidinyl)- (9CI) (CA INDEX NAME)

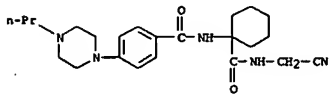


RN 354813-47-1 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-methyl-4-piperidinyl)- (9CI) (CA INDEX NAME)



RN 354813-50-6 CAPLUS

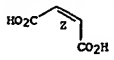
L11 ANSWER 22 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CRN 354813-19-7
CMF C23 H33 N5 O2



CM 2

CRN 110-16-7
CMF C4 H4 O4

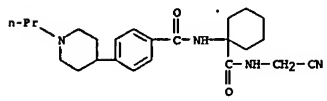
Double bond geometry as shown.



RN 843609-19-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-propyl-4-piperidinyl)-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

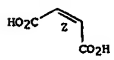
CRN 354813-31-3
CMF C24 H34 N4 O2



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



Karen Cheng

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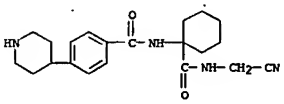
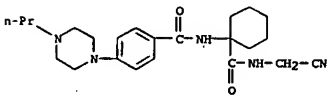
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)



RN 843609-17-6 CAPLUS
CN Phosphonic acid, [1-hydroxy-2-(1H-imidazol-1-yl)ethylidene]bis-, mixt. with N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)benzamide (9CI) (CA INDEX NAME)

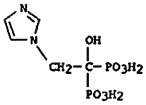
CM 1

CRN 354813-19-7
CMF C23 H33 N5 O2



CM 2

CRN 118072-93-8
CMF C5 H10 N2 O7 P2



RN 843609-18-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

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REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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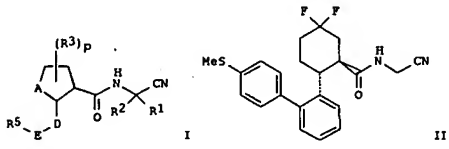
ACCESSION NUMBER: 2005:14363 CAPLUS
DOCUMENT NUMBER: 142:93425
TITLE: Preparation of N-(cyanomethyl)cycloalkanecarboxamides as cathepsin cysteine protease inhibitors for the treatment of osteoporosis and related diseases
INVENTOR(S): Bayly, Christopher; Black, Cameron; Crane, Sheldon; McKay, Daniel J.; Oballa, Renata; Robichaud, Joel
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000800	A1	20050106	WO 2004-CA948	20040628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004251794	A1	20050106	AU 2004-251794	20040628
CA 2530068	A1	20050106	CA 2004-2530068	20040628
EP 1644326	A1	20060412	EP 2004-737887	20040628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1812967	A	20060802	CN 2004-80018431	20040628
JP 2007505031	T	20070308	JP 2006-517916	20040628
PRIORITY APPLN. INFO.:			US 2003-483678P	P 20030630
			WO 2004-CA948	W 20040628

OTHER SOURCE(S): MARPAT 142:93425
GI



I

II

AB Title compds. I [wherein R1, R2 = H or (un)substituted alk(en)yl; R1 and R2 can link together; each R3 independently = H, halo or (un)substituted alkyl; two R3 can link together; D = alkyl; D, E = alkenyl, alkynyl, (un)substituted (hetero)aryl, cycloalkyl or heterocyclyl; R5 = H, alk(en/yn)yl, alkoxy, halo, nitro, cyano, (hetero)aryl, cycloalkyl, heterocyclyl or carbonyl, et al.; A = (CH2)n; n = 0-3; p = 0-3, or pharmaceutically acceptable salts, stereoisomers or N-oxide derivs. thereof] were prepared Examples include many N-(cyanomethyl)cyclohexanecarboxamides such as II. The invented compds. are cysteine protease inhibitors, including but not limited to, inhibitors of cathepsin K, L, S and B, with enhanced pharmacol. profiles (not data). Therefore, I and their pharmaceutical comps. are useful for treating diseases in which inhibition of bone resorption is indicated, such as osteoporosis.

IT 819858-00-9P 819858-01-0P 819858-02-1P 819858-56-5P, 2-(2-Bromophenyl)-N-(cyanomethyl)-5,5-difluorocyclohexanecarboxamide 819858-58-7P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-(methylthio)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-60-1P, N-(1-Cyanocyclopropyl)-5,5-difluoro-2-[4'-(methylthio)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-61-2P, 2-[4'-(Benzyloxy)-1,1'-biphenyl-2-yl]-N-(cyanomethyl)cyclohexanecarboxamide 819858-62-3P, N-(Cyanomethyl)-2-(4'-hydroxy-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-63-4P, N-(Cyanomethyl)-2-(4'-fluoro-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-64-5P, N-(Cyanomethyl)-2-[4'-(methylsulfonyl)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-65-6P, N-(Cyanomethyl)-5,5-difluoro-2-(4'-fluoro-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-66-7P, N-(Cyanomethyl)-2-(4'-vinyl-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-67-8P, N-(Cyanomethyl)-2-(4'-cyclopropyl-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-68-9P, N-(Cyanomethyl)-5,5-difluoro-2-[5-(methylsulfonyl)-4'-(methylthio)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-69-0P, N-(1-Cyanocyclopropyl)-5,5-difluoro-2-[5-(methylsulfonyl)-4'-(methylthio)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-70-3P, N-(Cyanomethyl)-2-[4'-[(fluoromethyl)thio]-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-71-4P, N-(Cyanomethyl)-2-(2'-methyl-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-72-5P, N-(Cyanomethyl)-2-(4'-methyl-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-73-6P, N-(Cyanomethyl)-2-(4'-ethyl-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-74-7P, N-(Cyanomethyl)-2-(4'-propyl-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-75-8P, N-(Cyanomethyl)-2-(3'-isopropyl-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-76-9P, N-(Cyanomethyl)-2-(4'-isopropyl-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-77-0P, 2-(4'-Tert-butyl-1,1'-biphenyl-2-yl)-N-(cyanomethyl)cyclohexanecarboxamide 819858-78-1P, N-(Cyanomethyl)-2-[3'-(trifluoromethyl)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-79-2P, N-(Cyanomethyl)-2-(3'-fluoro-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-80-5P, N-(Cyanomethyl)-2-(2'-fluoro-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-81-6P, 2-(4'-Chloro-1,1'-biphenyl-2-yl)-N-(cyanomethyl)cyclohexanecarboxamide 819858-82-7P, 2-(3'-Chloro-1,1'-biphenyl-2-yl)-N-(cyanomethyl)cyclohexanecarboxamide

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IT 819858-83-8P, N-(Cyanomethyl)-2-[3'-(hydroxymethyl)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-84-9P, 2'-[2-[[(Cyanomethyl)amino]carbonyl]cyclohexyl]-1,1'-biphenyl-3-carboxylic acid 819858-85-0P, 2'-[2-[[(Cyanomethyl)amino]carbonyl]cyclohexyl]-1,1'-biphenyl-4-carboxylic acid 819858-86-1P, N-(Cyanomethyl)-2-(3'-methoxy-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-87-2P, N-(Cyanomethyl)-2-(2'-ethoxy-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-88-3P, N-(Cyanomethyl)-2-(4'-ethoxy-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-89-4P, N-(Cyanomethyl)-2-(3'-isopropoxy-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-90-7P, N-(Cyanomethyl)-2-(4'-isopropoxy-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-91-8P, N-(Cyanomethyl)-2-(4'-phenoxy-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819858-92-9P, N-(Cyanomethyl)-2-(4'-(trifluoromethoxy)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-93-0P, N-(Cyanomethyl)-2-[2'-(methylthio)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-94-1P, N-(Cyanomethyl)-2-[3'-(methylthio)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-95-2P, N-(Cyanomethyl)-2-[4'-(ethylthio)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-96-3P, 2-(3'-Amino-1,1'-biphenyl-2-yl)-N-(cyanomethyl)cyclohexanecarboxamide 819858-98-5P, N-(Cyanomethyl)-2-[4'-(dimethylamino)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819858-99-6P, N-(Cyanomethyl)-2-(3'-nitro-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819859-00-2P, 2-[3'-(Acetylamino)-1,1'-biphenyl-2-yl]-N-(cyanomethyl)cyclohexanecarboxamide 819859-01-3P, N-(Cyanomethyl)-2-(4'-isobutyl-1,1'-biphenyl-2-yl)cyclohexanecarboxamide 819859-02-4P, N-(Cyanomethyl)-2-[2-(pyridin-4-yl)phenyl]cyclohexanecarboxamide 819859-03-5P, N-(Cyanomethyl)-2-[2-(quinolin-8-yl)phenyl]cyclohexanecarboxamide 819859-04-6P, N-(Cyanomethyl)-2-[2-(2-methoxypyrimidin-5-yl)phenyl]cyclohexanecarboxamide 819859-05-7P, N-(Cyanomethyl)-2-[2-(pyridin-3-yl)phenyl]cyclohexanecarboxamide 819859-06-8P, N-(Cyanomethyl)-2-[2-(thien-3-yl)phenyl]cyclohexanecarboxamide 819859-07-9P, 2-(4'-Acetyl-1,1'-biphenyl-2-yl)-N-(cyanomethyl)cyclohexanecarboxamide 819859-08-0P 819859-09-1P, 2-(4'-Cyano-1,1'-biphenyl-2-yl)-N-(cyanomethyl)cyclohexanecarboxamide 819859-10-4P, 2-(3'-Cyano-1,1'-biphenyl-2-yl)-N-(cyanomethyl)cyclohexanecarboxamide 819859-11-5P, 6-(3-Bromophenyl)-N-(cyanomethyl)cyclohex-3-ene-1-carboxamide 819859-12-6P, 2-(3-Bromophenyl)-N-(cyanomethyl)cyclohexanecarboxamide 819859-13-7P, tert-Butyl 4-[3'-[2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-1,1'-biphenyl-4-yl]piperazine-1-carboxylate 819859-14-8P, N-(Cyanomethyl)-2-[4'-(piperazin-1-yl)-1,1'-biphenyl-3-yl]cyclohexanecarboxamide 819859-15-9P, 2-(3-Bromophenyl)-N-(cyanomethyl)-4-methylcyclopentanecarboxamide 819859-16-0P, N-(Cyanomethyl)-2-(4'-methoxy-1,1'-biphenyl-3-yl)cyclohexanecarboxamide 819859-17-1P, N-(Cyanomethyl)-2-[4'-(methylthio)-1,1'-biphenyl-3-yl]cyclohexanecarboxamide 819859-18-2P, N-(Cyanomethyl)-2-[4'-(methylsulfonyl)-1,1'-biphenyl-3-yl]cyclohexanecarboxamide 819859-19-3P, N-(Cyanomethyl)-2-(5-phenyl-1,3-oxazol-2-yl)cyclohexanecarboxamide 819859-20-6P, N-(Cyanomethyl)-2-(5-phenyl-1,3-thiazol-2-yl)cyclohexanecarboxamide 819859-21-7P, 2-(2-Bromophenyl)-N-(cyanomethyl)cyclohexanecarboxamide 819859-22-8P, N-(Cyanomethyl)-2-[4'-(methylthio)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819859-23-9P, N-(Cyanomethyl)-2-phenylcyclohexanecarboxamide 819859-24-0P, N-(Cyanomethyl)-5,5-dichloro-2-[4'-(methylthio)-1,1'-biphenyl-2-yl]cyclohexanecarboxamide 819859-25-1P, N-(Cyanomethyl)-5,5-difluoro-2-[1-methyl-3-[4-(methylthio)phenyl]-1H-pyrazol-4-yl]cyclohexanecarboxamide

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IT 819859-26-2P, 6-(2-Bromophenyl)-N-(cyanomethyl)spiro[2.5]octane-5-carboxamide 819859-27-3P, 2-(3-Bromo-1-methyl-1H-pyrazol-4-yl)-N-(cyanomethyl)-5,5-difluorocyclohexanecarboxamide 819859-28-4P, N-(Cyanomethyl)-6-[4'-(methylthio)-1,1'-biphenyl-2-yl]spiro[2.5]octane-5-carboxamide 819859-29-5P, 2-(2-Bromophenyl)-5,5-dichloro-N-(cyanomethyl)cyclohexanecarboxamide 819859-30-8P, 2-(3-Bromo-1-methyl-1H-pyrazol-4-yl)-5,5-dichloro-N-(cyanomethyl)cyclohexanecarboxamide 819859-31-9P 819859-32-0P, N-(Cyanomethyl)-2-[2-[4-(methylthio)phenyl]ethyl]cyclohexanecarboxamide 819859-33-1P 819859-34-2P, N-(Cyanomethyl)-2-[2-[4-(methylsulfonyl)phenyl]ethyl]cyclohexanecarboxamide 819859-35-3P 819859-36-4P 819859-37-5P, N-(Cyanomethyl)-2-[2-[4-[(trifluoromethyl)thio]phenyl]ethyl]cyclohexanecarboxamide 819859-38-6P, N-(Cyanomethyl)-2-ethynylcyclohexanecarboxamide 819859-39-7P, N-(Cyanomethyl)-2-[[4-(methylthio)phenyl]ethynyl]cyclohexanecarboxamide 819859-40-0P, N-(Cyanomethyl)-2-[[4-(methylsulfonyl)phenyl]ethynyl]cyclohexanecarboxamide 819859-41-1P, N-(Cyanomethyl)-2-[[4-[(trifluoromethyl)thio]phenyl]ethynyl]cyclohexanecarboxamide 819859-42-2P, N-(Cyanomethyl)-2-(phenylethynyl)cyclohexanecarboxamide 819859-43-3P, 2-[[4-Bromophenyl)ethynyl]-N-(cyanomethyl)cyclohexanecarboxamide 819859-44-4P, 2-[[1,1'-Biphenyl-4-yl)ethynyl]-N-(cyanomethyl)cyclohexanecarboxamide 819859-45-5P, N-(Cyanomethyl)-2-[[4'-(methylthio)-1,1'-biphenyl-4-yl]ethynyl]cyclohexanecarboxamide 819859-46-6P, N-(Cyanomethyl)-2-[(3-fluorophenyl)ethynyl]cyclohexanecarboxamide 819859-47-7P, 2-[(3-Chlorophenyl)ethynyl]-N-(cyanomethyl)cyclohexanecarboxamide 819859-48-8P, N-(Cyanomethyl)-2-[[4-(pyridin-4-yl)phenyl]ethynyl]cyclohexanecarboxamide 819859-49-9P, 2-[(3-Bromophenyl)ethynyl]-N-(cyanomethyl)cyclohexanecarboxamide 819859-50-2P, 2-[(1,1'-Biphenyl-3-yl)ethynyl]-N-(cyanomethyl)cyclohexanecarboxamide 819859-51-3P, 2-[(2-Bromophenyl)ethynyl]-N-(cyanomethyl)cyclohexanecarboxamide 819859-52-4P, 2-[(1,1'-Biphenyl-2-yl)ethynyl]-N-(cyanomethyl)cyclohexanecarboxamide 819859-53-5P, N-(Cyanomethyl)-2-[[4-(6-methoxypyridin-2-yl)thien-3-yl]ethynyl]cyclohexanecarboxamide 819859-54-6P, N-(Cyanomethyl)-2-[4'-[(cyanomethyl)thio]biphenyl-2-yl]-5,5-difluorocyclohexanecarboxamide 819859-55-7P, 2-[4'-[(2-Amino-2-oxoethyl)thio]biphenyl-2-yl]-N-(cyanomethyl)-5,5-difluorocyclohexanecarboxamide 819859-56-8P, N-(Cyanomethyl)-2-[4'-[[2-[(cyanomethyl)amino]-2-oxoethyl]thio]biphenyl-2-yl]-5,5-difluorocyclohexanecarboxamide 819859-57-9P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[2-(pyridin-2-yl)ethyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-58-0P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[(pyridin-2-ylmethyl)thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-59-1P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[(pyridin-3-ylmethyl)thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-60-4P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[(pyridin-4-ylmethyl)thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-61-5P, 2-[4'-[(1H-Benzimidazol-2-ylmethyl)thio]biphenyl-2-yl]-N-(cyanomethyl)-5,5-difluorocyclohexanecarboxamide 819859-62-6P, 2-[4'-[(1H-Benzimidazol-6-ylmethyl)thio]biphenyl-2-yl]-N-(cyanomethyl)-5,5-difluorocyclohexanecarboxamide 819859-63-7P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[(1H-imidazol-4-ylmethyl)thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-64-8P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[(1H-imidazol-2-ylmethyl)thio]biphenyl-2-

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yl]cyclohexanecarboxamide 819859-65-9P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[[1-(1H-imidazol-2-ylmethyl)-1H-imidazol-2-yl]methyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-66-0P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[2-(1H-imidazol-4-yl)ethyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-67-1P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[2-(1H-imidazol-2-yl)ethyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-68-2P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[(1-methylpiperidin-4-yl)methyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-69-3P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[2-(1-methylpiperidin-4-yl)ethyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-70-6P, N-(Cyanomethyl)-5,5-difluoro-2-[2'-fluoro-4'-(methylthio)biphenyl-2-yl]cyclohexanecarboxamide 819859-71-7P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[(5-phenyl-1H-imidazol-2-yl)methyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-72-8P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[2-(pyridin-4-yl)ethyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-73-9P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[2-[(pyridin-2-ylsulfonyl)amino]ethyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-74-0P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[2-[(pyridin-2-ylsulfonyl)[2-[[(pyridin-2-yl)sulfonyl]amino]ethyl]amino]ethyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-75-1P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[(1H-tetrazol-5-ylmethyl)thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-76-2P, 2-[4'-[(1-Cyanocyclopropyl)thio]biphenyl-2-yl]-N-(cyanomethyl)-5,5-difluorocyclohexanecarboxamide 819859-77-3P, 1-[[2'-[2-[[(Cyanomethyl)amino]carbonyl]-4,4-difluorocyclohexyl]biphenyl-4-yl]thio]cyclopropanecarboximidic acid methyl ester 819859-78-4P, 2-[4'-[[2-(1H-Benzimidazol-2-yl)ethyl]thio]biphenyl-2-yl]-N-(cyanomethyl)-5,5-difluorocyclohexanecarboxamide 819859-79-5P, 2-[4'-[(1H-Benzimidazol-7-ylmethyl)thio]biphenyl-2-yl]-N-(cyanomethyl)-5,5-difluorocyclohexanecarboxamide 819859-80-8P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[[2-[(methylsulfonyl)amino]ethyl]thio]biphenyl-2-yl]cyclohexanecarboxamide 819859-81-9P, N-(Cyanomethyl)-5,5-difluoro-2-[4'-[2-[(methylsulfonyl)amino]ethyl]biphenyl-2-yl]cyclohexanecarboxamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(inhibitor; prepn. of (cyanomethyl)cyclohexanecarboxamides as cathepsin cysteine protease inhibitors)

RN 819858-00-9 CAPLUS

CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

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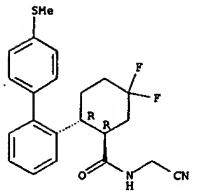
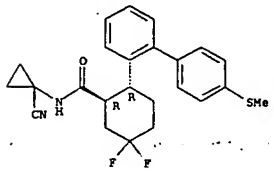


RN 819858-01-0 CAPLUS

CN Cyclohexanecarboxamide, N-(1-cyanocyclopropyl)-5,5-difluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

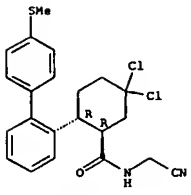


RN 819858-02-1 CAPLUS

CN Cyclohexanecarboxamide, 5,5-dichloro-N-(cyanomethyl)-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

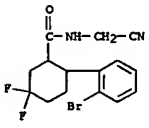
Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



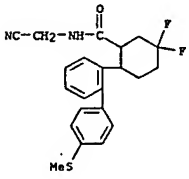
RN 819858-56-5 CAPLUS

CN Cyclohexanecarboxamide, 2-(2-bromophenyl)-N-(cyanomethyl)-5,5-difluoro- (9CI) (CA INDEX NAME)



RN 819858-58-7 CAPLUS

CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819858-60-1 CAPLUS

CN Cyclohexanecarboxamide, N-(1-cyanocyclopropyl)-5,5-difluoro-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

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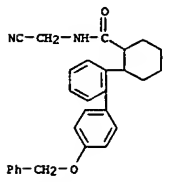
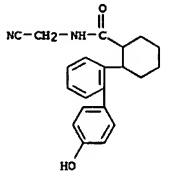
RN 819858-61-2 CAPLUS

CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(phenylmethoxy)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819858-62-3 CAPLUS

CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-hydroxy[1,1'-biphenyl]-2-yl)- (9CI) (CA INDEX NAME)



RN 819858-63-4 CAPLUS

CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-fluoro[1,1'-biphenyl]-2-yl)- (9CI) (CA INDEX NAME)

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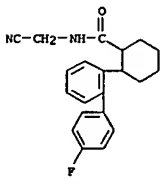
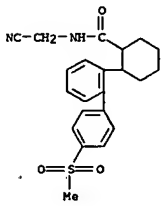
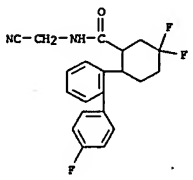


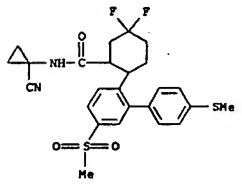
RN 819858-64-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(methylsulfonyl)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



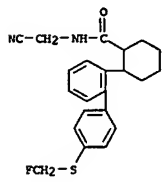
RN 819858-65-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-(4'-fluoro[1,1'-biphenyl]-2-yl)- (9CI) (CA INDEX NAME)



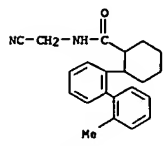
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN . (Continued)
(methylsulfonyl)-4'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819858-70-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-[(fluoromethyl)thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819858-71-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(2'-methyl[1,1'-biphenyl]-2-yl)- (9CI) (CA INDEX NAME)



RN 819858-72-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-methyl[1,1'-biphenyl]-2-yl)- (9CI) (CA INDEX NAME)

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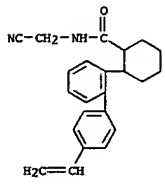
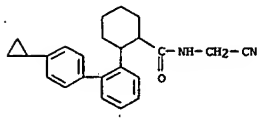
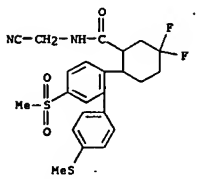
RN 819858-66-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-ethenyl[1,1'-biphenyl]-2-yl)- (9CI) (CA INDEX NAME)



RN 819858-67-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-cyclopropyl[1,1'-biphenyl]-2-yl)- (9CI) (CA INDEX NAME)

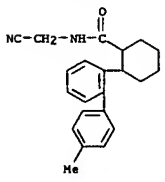


RN 819858-68-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[5-(methylsulfonyl)-4'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

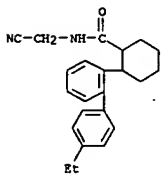


RN 819858-69-0 CAPLUS
CN Cyclohexanecarboxamide, N-(1-cyanocyclopropyl)-5,5-difluoro-2-[5-

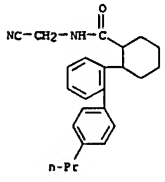
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-73-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-ethyl[1,1'-biphenyl]-2-yl)- (9CI) (CA INDEX NAME)

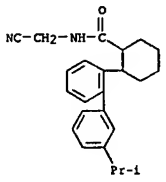


RN 819858-74-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-propyl[1,1'-biphenyl]-2-yl)- (9CI) (CA INDEX NAME)

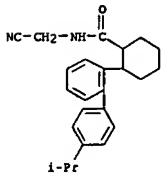


RN 819858-75-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[3'-(1-methylethyl)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

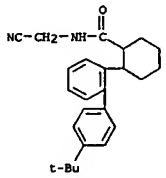
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-76-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(1-methylethyl)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

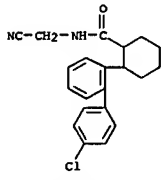


RN 819858-77-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(1,1-dimethylethyl)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

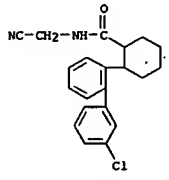


RN 819858-78-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[3'-(trifluoromethyl)[1,1'-

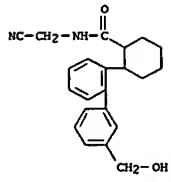
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-82-7 CAPLUS
CN Cyclohexanecarboxamide, 2-(3'-chloro[1,1'-biphenyl]-2-yl)-N-(cyanomethyl)-(9CI) (CA INDEX NAME)

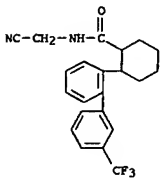


RN 819858-83-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[3'-(hydroxymethyl)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

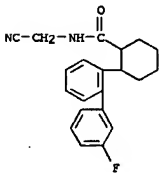


RN 819858-84-9 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 2'-[2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

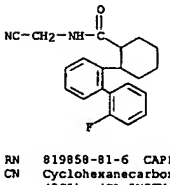
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819858-79-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(3'-fluoro[1,1'-biphenyl]-2-yl)-(9CI) (CA INDEX NAME)

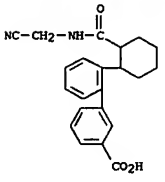


RN 819858-80-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(2'-fluoro[1,1'-biphenyl]-2-yl)-(9CI) (CA INDEX NAME)

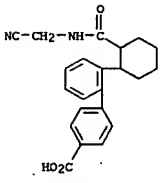


RN 819858-81-6 CAPLUS
CN Cyclohexanecarboxamide, 2-(4'-chloro[1,1'-biphenyl]-2-yl)-N-(cyanomethyl)-(9CI) (CA INDEX NAME)

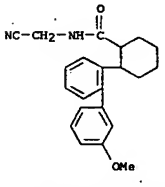
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-85-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 2'-[2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)



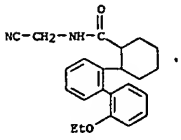
RN 819858-86-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(3'-methoxy[1,1'-biphenyl]-2-yl)-(9CI) (CA INDEX NAME)



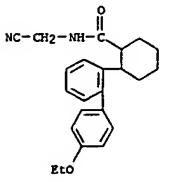
RN 819858-87-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(2'-ethoxy[1,1'-biphenyl]-2-yl)-(9CI) (CA INDEX NAME)

Karen Cheng

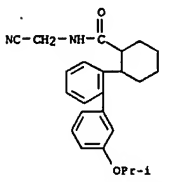
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-88-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-ethoxy[1,1'-biphenyl]-2-yl)-(9CI) (CA INDEX NAME)

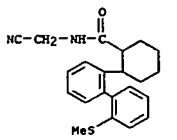


RN 819858-89-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[3'-(1-methylethoxy)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

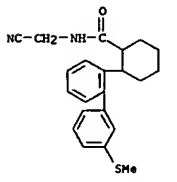


RN 819858-90-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(1-methylethoxy)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

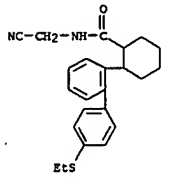
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-94-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[3'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

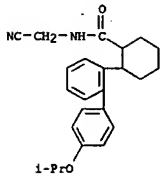


RN 819858-95-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(ethylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

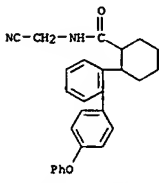


RN 819858-96-3 CAPLUS
CN Cyclohexanecarboxamide, 2-(3'-amino[1,1'-biphenyl]-2-yl)-N-(cyanomethyl)-(9CI) (CA INDEX NAME)

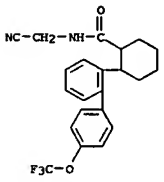
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-91-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-phenoxy[1,1'-biphenyl]-2-yl)-(9CI) (CA INDEX NAME)

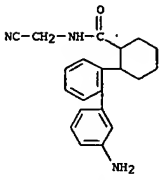


RN 819856-92-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(trifluoromethoxy)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

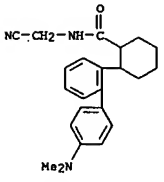


RN 819858-93-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

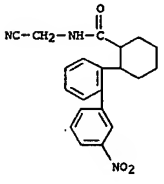
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-98-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(dimethylamino)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

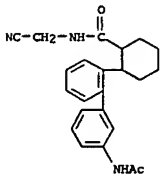


RN 819858-99-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(3'-nitro[1,1'-biphenyl]-2-yl)-(9CI) (CA INDEX NAME)

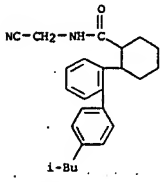


RN 819859-00-2 CAPLUS
CN Cyclohexanecarboxamide, 2-[3'-(acetylamino)[1,1'-biphenyl]-2-yl]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

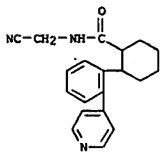
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-01-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(2-methylpropyl)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

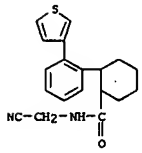


RN 819859-02-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2-(4-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)

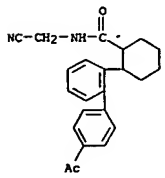


RN 819859-03-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2-(8-quinolinyl)phenyl]- (9CI) (CA INDEX NAME)

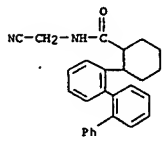
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-07-9 CAPLUS
CN Cyclohexanecarboxamide, 2-(4'-acetyl[1,1'-biphenyl]-2-yl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

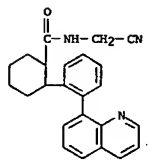


RN 819859-08-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[1,1':2',1''-terphenyl]-2-yl- (9CI) (CA INDEX NAME)

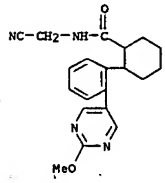


RN 819859-09-1 CAPLUS
CN Cyclohexanecarboxamide, 2-(4'-cyano[1,1'-biphenyl]-2-yl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

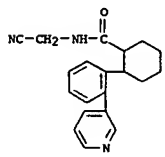
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-04-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2-(2-methoxy-5-pyrimidinyl)phenyl]- (9CI) (CA INDEX NAME)

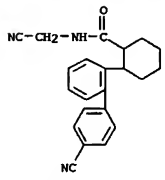


RN 819859-05-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)

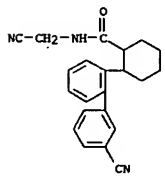


RN 819859-06-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2-(3-thienyl)phenyl]- (9CI) (CA INDEX NAME)

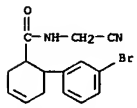
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-10-4 CAPLUS
CN Cyclohexanecarboxamide, 2-(3'-cyano[1,1'-biphenyl]-2-yl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

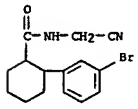


RN 819859-11-5 CAPLUS
CN 3-Cyclohexene-1-carboxamide, 6-(3-bromophenyl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

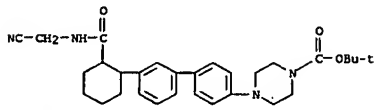


RN 819859-12-6 CAPLUS
CN Cyclohexanecarboxamide, 2-(3-bromophenyl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

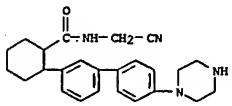
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



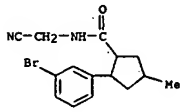
RN 819859-13-7 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[3'-[2-[[(cyanomethyl)amino]carbonyl]cycloh exyl][1,1'-biphenyl]-4-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 819859-14-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(1-piperazinyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

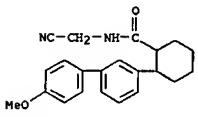


RN 819859-15-9 CAPLUS
CN Cyclopentanecarboxamide, 2-(3-bromophenyl)-N-(cyanomethyl)-4-methyl- (9CI) (CA INDEX NAME)

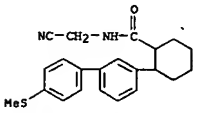


RN 819859-16-0 CAPLUS

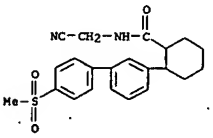
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(4'-methoxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



RN 819859-17-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(methylthio)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

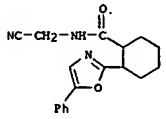


RN 819859-18-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(methylsulfonyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

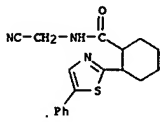


RN 819859-19-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(5-phenyl-2-oxazolyl)- (9CI) (CA INDEX NAME)

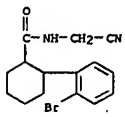
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



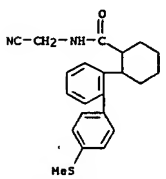
RN 819859-20-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(5-phenyl-2-thiazolyl)- (9CI) (CA INDEX NAME)



RN 819859-21-7 CAPLUS
CN Cyclohexanecarboxamide, 2-(2-bromophenyl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

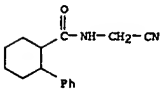


RN 819859-22-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

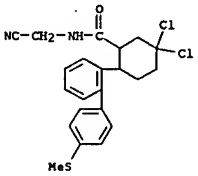


L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

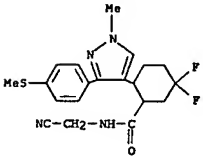
RN 819859-23-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-phenyl- (9CI) (CA INDEX NAME)



RN 819859-24-0 CAPLUS
CN Cyclohexanecarboxamide, 5,5-dichloro-N-(cyanomethyl)-2-(4'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819859-25-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[1-methyl-3-[4-(methylthio)phenyl]-1H-pyrazol-4-yl]- (9CI) (CA INDEX NAME)



RN 819859-26-2 CAPLUS
CN Spiro[2.5]octane-5-carboxamide, 6-(2-bromophenyl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

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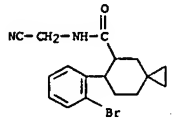
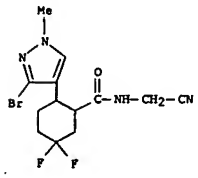
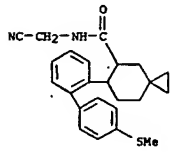
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-27-3 CAPLUS
CN Cyclohexanecarboxamide, 2-(3-bromo-1-methyl-1H-pyrazol-4-yl)-N-(cyanomethyl)-5,5-difluoro- (9CI) (CA INDEX NAME)

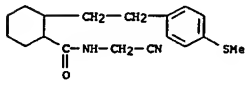


RN 819859-28-4 CAPLUS
CN Spiro[2.5]octane-5-carboxamide, N-(cyanomethyl)-6-[4'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



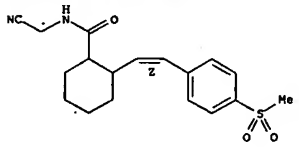
RN 819859-29-5 CAPLUS
CN Cyclohexanecarboxamide, 2-(2-bromophenyl)-5,5-dichloro-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

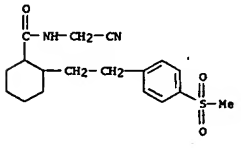


RN 819859-33-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(1Z)-2-[4-(methylsulfonyl)phenyl]ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

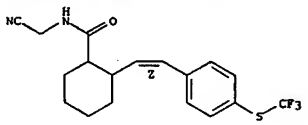


RN 819859-34-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2-[4-(methylsulfonyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



RN 819859-35-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(1Z)-2-[4-[(trifluoromethyl)thio]phenyl]ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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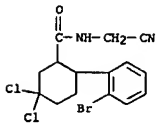
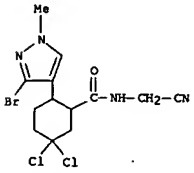
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

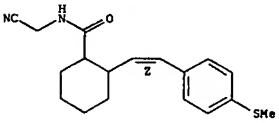


RN 819859-30-8 CAPLUS
CN Cyclohexanecarboxamide, 2-(3-bromo-1-methyl-1H-pyrazol-4-yl)-5,5-dichloro-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



RN 819859-31-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(1Z)-2-[4-(methylthio)phenyl]ethenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

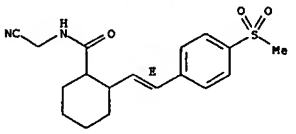


RN 819859-32-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2-[4-(methylthio)phenyl]ethyl]- (9CI) (CA INDEX NAME)

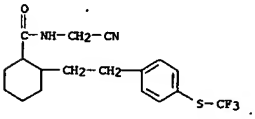
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 819859-36-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(1E)-2-[4-(methylsulfonyl)phenyl]ethenyl]- (9CI) (CA INDEX NAME)

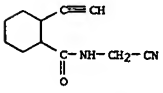
Double bond geometry as shown.



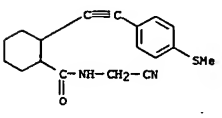
RN 819859-37-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[2-[4-[(trifluoromethyl)thio]phenyl]ethyl]- (9CI) (CA INDEX NAME)



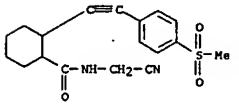
RN 819859-38-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-ethynyl- (9CI) (CA INDEX NAME)



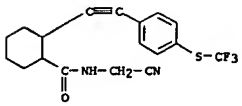
RN 819859-39-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[4-(methylthio)phenyl]ethynyl]- (9CI) (CA INDEX NAME)



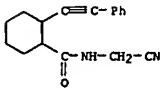
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 819859-40-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[4-(methylsulfonyl)phenyl]ethynyl]- (9CI) (CA INDEX NAME)



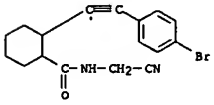
RN 819859-41-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[4-[(trifluoromethyl)thio]phenyl]ethynyl]- (9CI) (CA INDEX NAME)



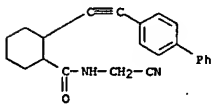
RN 819859-42-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(phenylethynyl)- (9CI) (CA INDEX NAME)



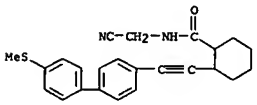
RN 819859-43-3 CAPLUS
CN Cyclohexanecarboxamide, 2-[(4-bromophenyl)ethynyl]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



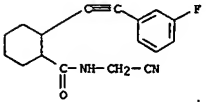
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 819859-44-4 CAPLUS
CN Cyclohexanecarboxamide, 2-([1,1'-biphenyl]-4-ylethynyl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



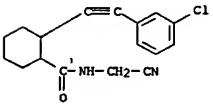
RN 819859-45-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[4'-(methylthio)[1,1'-biphenyl]-4-yl]ethynyl]- (9CI) (CA INDEX NAME)



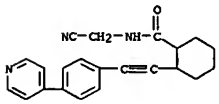
RN 819859-46-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(3-fluorophenyl)ethynyl]- (9CI) (CA INDEX NAME)



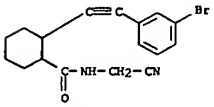
RN 819859-47-7 CAPLUS
CN Cyclohexanecarboxamide, 2-[(3-chlorophenyl)ethynyl]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



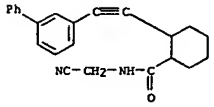
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 819859-48-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(4-(4-pyridinyl)phenyl]ethynyl]- (9CI) (CA INDEX NAME)



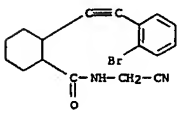
RN 819859-49-9 CAPLUS
CN Cyclohexanecarboxamide, 2-[(3-bromophenyl)ethynyl]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



RN 819859-50-2 CAPLUS
CN Cyclohexanecarboxamide, 2-([1,1'-biphenyl]-3-ylethynyl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

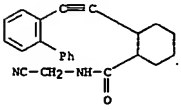


RN 819859-51-3 CAPLUS
CN Cyclohexanecarboxamide, 2-[(2-bromophenyl)ethynyl]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

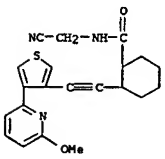


RN 819859-52-4 CAPLUS

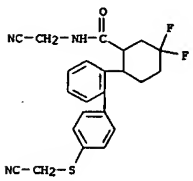
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Cyclohexanecarboxamide, 2-([1,1'-biphenyl]-2-ylethynyl)-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



RN 819859-53-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[4-(6-methoxy-2-pyridinyl)-3-thienyl]ethynyl]- (9CI) (CA INDEX NAME)



RN 819859-54-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-[(cyanomethyl)thio][1,1'-biphenyl]-2-yl]-5,5-difluoro- (9CI) (CA INDEX NAME)



RN 819859-55-7 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(2-amino-2-oxoethyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro- (9CI) (CA INDEX NAME)

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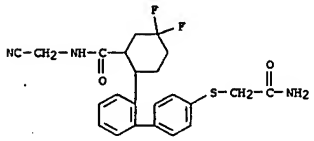
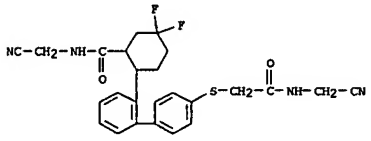
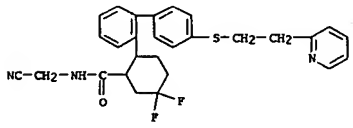
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-56-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-[[2-[(cyanomethyl)amino]-2-oxoethyl]thio][1,1'-biphenyl]-2-yl]-5,5-difluoro- (9CI) (CA INDEX NAME)

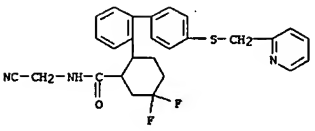


RN 819859-57-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(2-pyridinyl)ethyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

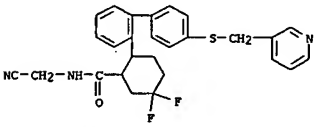


RN 819859-58-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(2-pyridinylmethyl)thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

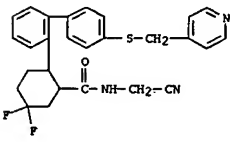
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-59-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(3-pyridinylmethyl)thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

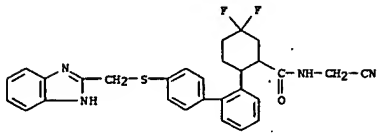


RN 819859-60-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(4-pyridinylmethyl)thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

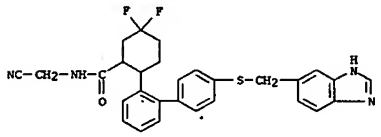


RN 819859-61-5 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(1H-benzimidazol-2-ylmethyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro- (9CI) (CA INDEX NAME)

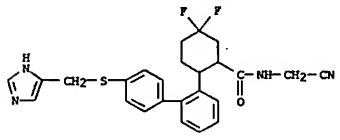
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



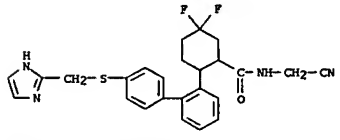
RN 819859-62-6 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(1H-benzimidazol-5-ylmethyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro- (9CI) (CA INDEX NAME)



RN 819859-63-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(1H-imidazol-4-ylmethyl)thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

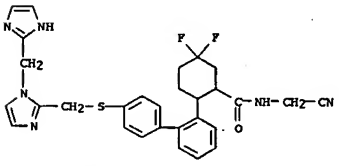


RN 819859-64-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(1H-imidazol-2-ylmethyl)thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

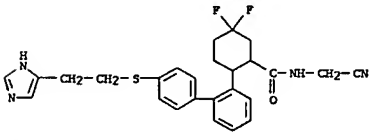


L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

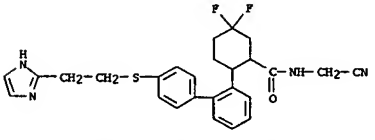
RN 819859-65-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[[1-(1H-imidazol-2-ylmethyl)-1H-imidazol-2-yl]methyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819859-66-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(1H-imidazol-4-yl)ethyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819859-67-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(1H-imidazol-2-yl)ethyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819859-68-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[(1-methyl-4-piperidinyl)methyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

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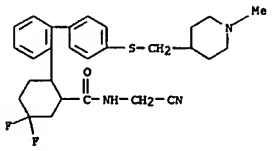
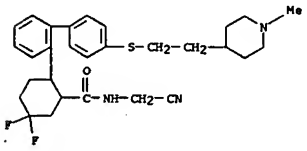
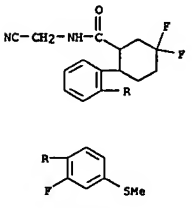
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-69-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(1-methyl-4-piperidinyl)ethyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

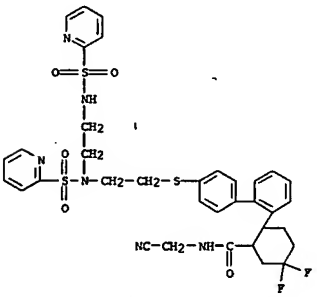


RN 819859-70-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[2'-fluoro-4'-(methylthio)[1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

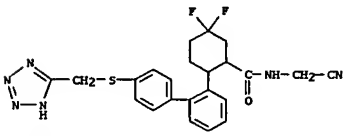


RN 819859-71-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[(4-phenyl-1H-imidazol-2-yl)methyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

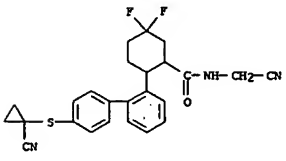
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-75-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(1H-tetrazol-5-ylmethyl)thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



RN 819859-76-2 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(1-cyanocyclopropyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro- (9CI) (CA INDEX NAME)



RN 819859-77-3 CAPLUS

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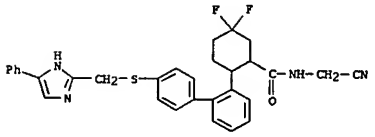
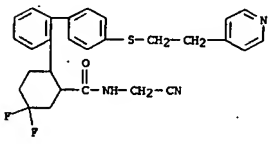
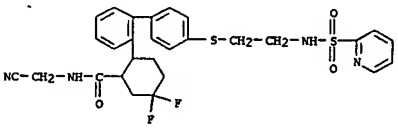
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819859-72-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(4-pyridinyl)ethyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



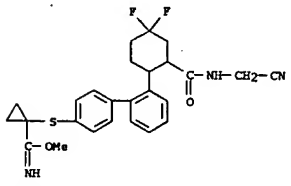
RN 819859-73-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-[(2-pyridinylsulfonyl)amino]ethyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



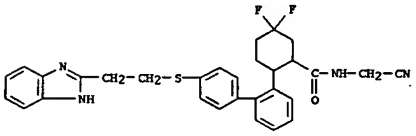
RN 819859-74-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-[(2-pyridinylsulfonyl)[2-[(2-pyridinylsulfonyl)amino]ethyl]amino]ethyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

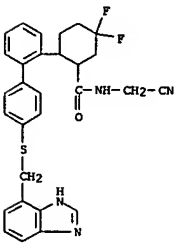
CN Cyclopropanecarboximidic acid, 1-[[2'-[2-[[(cyanomethyl)amino]carbonyl]-4,4-difluorocyclohexyl][1,1'-biphenyl]-4-yl]thio]-, methyl ester (9CI) (CA INDEX NAME)



RN 819859-78-4 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[[2-(1H-benzimidazol-2-yl)ethyl]thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro- (9CI) (CA INDEX NAME)

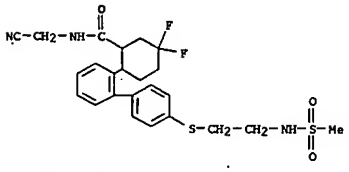


RN 819859-79-5 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(1H-benzimidazol-4-ylmethyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro- (9CI) (CA INDEX NAME)

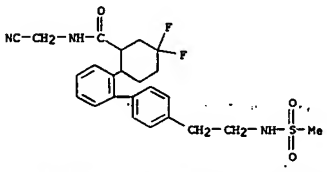


L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 819859-80-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-[(methylsulfonyl)amino]ethyl]thio][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



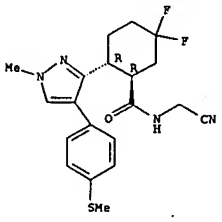
RN 819859-81-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[2-[(methylsulfonyl)amino]ethyl][1,1'-biphenyl]-2-yl]- (9CI) (CA INDEX NAME)



IT 819858-04-3P 819858-06-5P 819858-08-7P
819858-10-1P 819858-12-3P 819858-14-5P
819858-16-7P 819858-18-9P 819858-20-3P
819858-22-5P 819858-24-7P 819858-26-9P
819858-27-0P 819858-28-1P 819858-29-2P
819858-30-5P 819858-31-6P 819858-32-7P
819858-33-8P 819858-34-9P 819858-35-0P
819858-36-1P 819858-37-2P 819858-38-3P
819858-39-4P 819858-40-7P 819858-41-8P
819858-42-9P 819858-43-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (cyanomethyl)cyclohexanecarboxamides as cathepsin cysteine
protease inhibitors)
RN 819858-04-3 CAPLUS

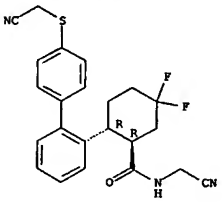
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[1-methyl-4-[4-(methylthio)phenyl]-1H-pyrazol-3-yl]-, (1R,2R)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 819858-06-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[4'-[(cyanomethyl)thio][1,1'-biphenyl]-2-yl]-5,5-difluoro-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

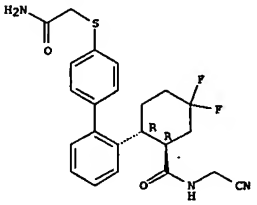
Relative stereochemistry.



RN 819858-08-7 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(2-amino-2-oxoethyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

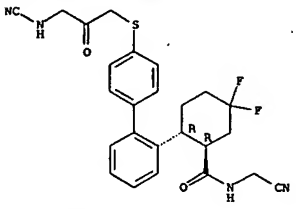
Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-10-1 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[[3-(cyanoamino)-2-oxopropyl]thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

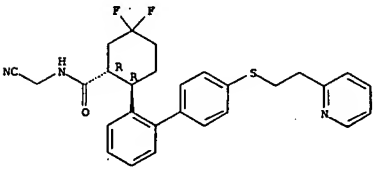
Relative stereochemistry.



RN 819858-12-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(2-pyridinyl)ethyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

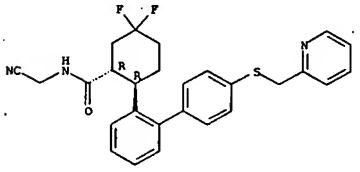
Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



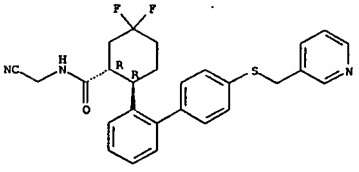
RN 819858-14-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(2-pyridinylmethyl)thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 819858-16-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(3-pyridinylmethyl)thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

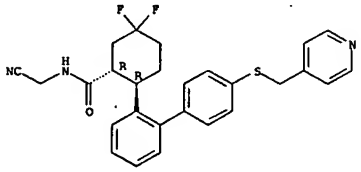
Relative stereochemistry.



RN 819858-18-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(4-

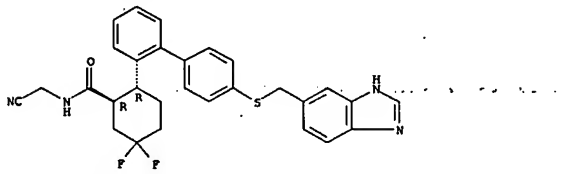
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
pyridinylmethyl)thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 819858-20-3 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(1H-benzimidazol-5-ylmethyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

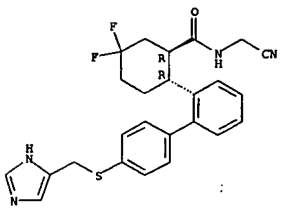
Relative stereochemistry.



RN 819858-22-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(1H-imidazol-4-ylmethyl)thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

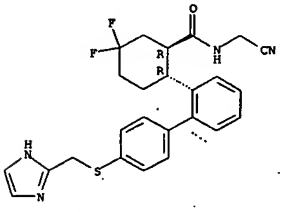
Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-24-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(1H-imidazol-2-ylmethyl)thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

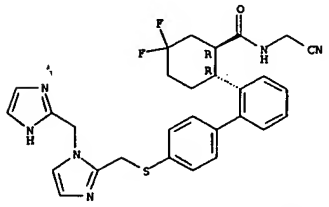
Relative stereochemistry.



RN 819858-26-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[[1-(1H-imidazol-2-ylmethyl)-1H-imidazol-2-yl]methyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

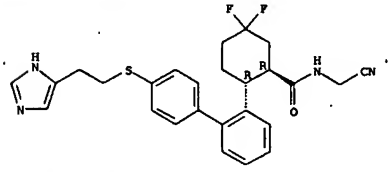
Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



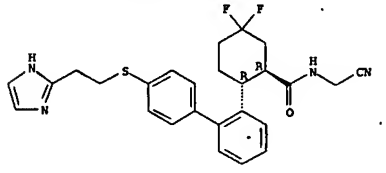
RN 819858-27-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(1H-imidazol-4-yl)ethyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



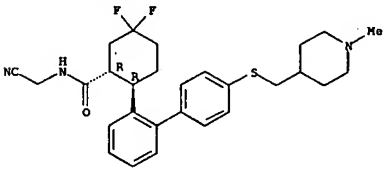
RN 819858-28-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(1H-imidazol-2-yl)ethyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



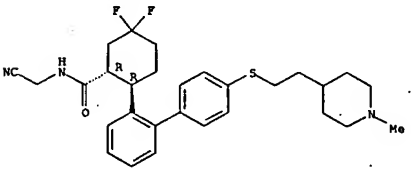
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 819858-29-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[(1-methyl-4-piperidinyl)methyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 819858-30-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(1-methyl-4-piperidinyl)ethyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

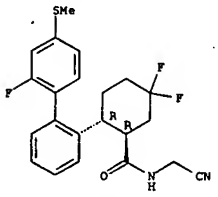


RN 819858-31-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[2'-fluoro-4'-(methylthio)[1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

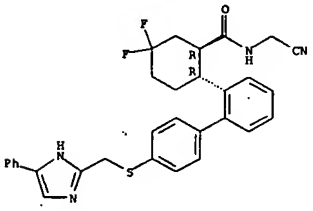
Karen Cheng

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-32-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[(4-phenyl-1H-imidazol-2-yl)methyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

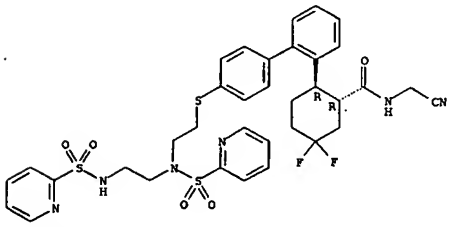
Relative stereochemistry.



RN 819858-33-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-(4-pyridinyl)ethyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

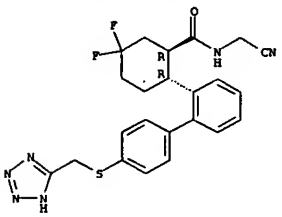
Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-36-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[(1H-tetrazol-5-ylmethyl)thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

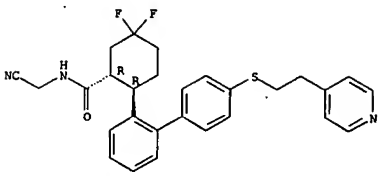
Relative stereochemistry.



RN 819858-37-2 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(1-cyanocyclopropyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

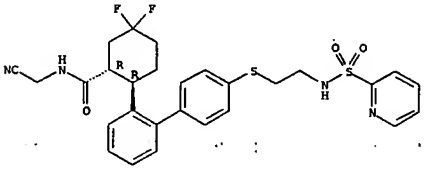
Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-34-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-[(2-pyridinylsulfonyl)amino]ethyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

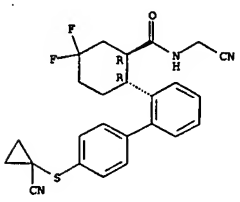
Relative stereochemistry.



RN 819858-35-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-[(2-pyridinylsulfonyl)[2-[(2-pyridinylsulfonyl)amino]ethyl]amino]ethyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

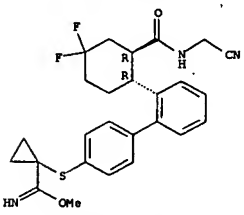
Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-38-3 CAPLUS
CN Cyclopropanecarboximidic acid, 1-[[2'-[(1R,2R)-2-[[(cyanomethyl)amino]carbonyl]-4,4-difluorocyclohexyl][1,1'-biphenyl]-4-yl]thio]-, methyl ester, rel- (9CI) (CA INDEX NAME)

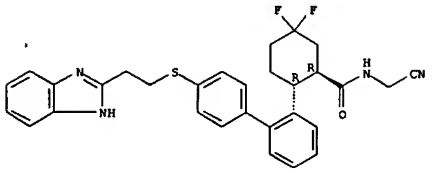
Relative stereochemistry.



RN 819858-39-4 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(2-(1H-benzimidazol-2-yl)ethyl]thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

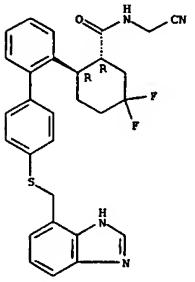
Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-40-7 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(1H-benzimidazol-4-ylmethyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

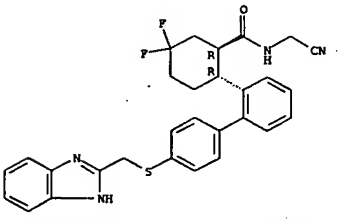
Relative stereochemistry.



RN 819858-41-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[[2-[(methylsulfonyl)amino]ethyl]thio][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

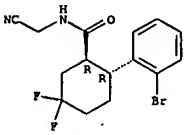
L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 819858-51-0P, (1R,2R)-2-(2-Bromophenyl)-N-(cyanomethyl)-5,5-difluorocyclohexanecarboxamide 819858-52-1P, (1R,2R)-2-(2-Bromophenyl)-N-(1-cyanocyclopropyl)-5,5-difluorocyclohexanecarboxamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (cyanomethyl)cyclohexanecarboxamides as cathepsin cysteine protease inhibitors)

RN 819858-51-0 CAPLUS
CN Cyclohexanecarboxamide, 2-(2-bromophenyl)-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)- (9CI) (CA INDEX NAME)

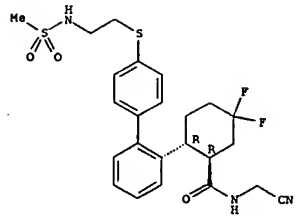
Absolute stereochemistry.



RN 819858-52-1 CAPLUS
CN Cyclohexanecarboxamide, 2-(2-bromophenyl)-N-(1-cyanocyclopropyl)-5,5-difluoro-, (1R,2R)- (9CI) (CA INDEX NAME)

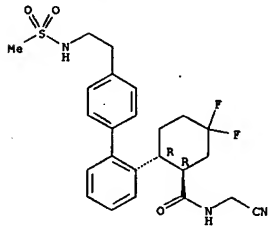
Absolute stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 819858-42-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-5,5-difluoro-2-[4'-[2-[(methylsulfonyl)amino]ethyl][1,1'-biphenyl]-2-yl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

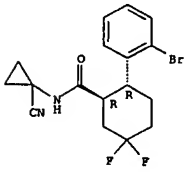
Relative stereochemistry.



RN 819858-43-0 CAPLUS
CN Cyclohexanecarboxamide, 2-[4'-[(1H-benzimidazol-2-ylmethyl)thio][1,1'-biphenyl]-2-yl]-N-(cyanomethyl)-5,5-difluoro-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L11 ANSWER 23 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Karen Cheng

L11 ANSWER 24 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1127383 CAPLUS
DOCUMENT NUMBER: 142:74617
TITLE: Imidazotriazinone derivatives as PDE 7 (phosphodiesterase 7) inhibitors, their preparation, and pharmaceutical compositions containing them
INVENTOR(S): Inoue, Hidekazu; Murafuji, Hidenobu; Hayashi, Yasuharu
PATENT ASSIGNEE(S): Daiichi Suntory Pharma Co.,ltd., Japan; Daiichi Suntory Biomedical Research Co.,ltd.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111053	A1	20041223	WO 2004-JP8642	20040611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
JP 2006219374	A	20060824	JP 2003-170095	20030613
EP 1636234	A1	20060322	EP 2004-736703	20040611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2006128707	A1	20060615	US 2005-560503	20051213
PRIORITY APPLN. INFO.:			JP 2003-170095 A	20030613
			WO 2004-JP8642 W	20040611

OTHER SOURCE(S): MARPAT 142:74617
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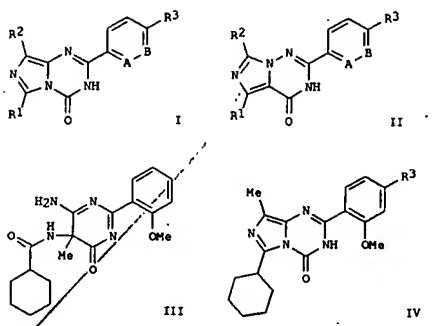
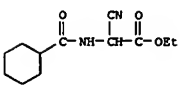


L11 ANSWER 24 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

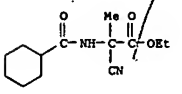
AB The invention provides compds. which inhibit PDE 7 selectively, and therefore enhance cellular cAMP levels. Consequently, the compds. are useful for treating various kinds of diseases, such as allergic diseases, inflammatory diseases, or immunol. diseases. The compds. are imidazotriazinones I and II [wherein: A is N or CR4; B is N or CH; R1 is (un)substituted cycloalkyl or tert-Bu; R2 is H or C1-C6 alkyl; R3 is H, NO2, cyano, halo, heteroaryl, (un)substituted C1-C6 alkyl, (un)substituted C2-C6 alkenyl, (un)saturated (un)substituted heterocycloalkyl, NR5R6, COR7, SO2R7, OR8, NR8COR7, NR8SO2R7; R4 is H or C1-C3 alkoxy group which is (un)substituted by one or more F atom(s); R5 and R6 are (independently) H, (un)substituted C1-C6 alkyl, (un)substituted acyl, or (un)substituted heterocycloalkyl; R7 is H, (un)substituted C1-C6 alkyl group, (un)substituted heterocycloalkyl, OH, OR8, or NR5R6; R8 is H, (un)substituted C1-C6 alkyl, or (un)substituted heterocycloalkyl; or pharmaceutically acceptable salts or solvates]. The compds. include particularly I and II [wherein: R1 is cyclohexyl; R2 is Me; R3 is H, NO2, cyano, halo, heteroaryl, (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, (un)saturated heterocycloalkyl, NR5R6, COR7, SO2R7, OR8, NR8COR7, NR8SO2R7; A is CR4; and B is CH]. The prepared compds. include 4 invention compds. and 8 intermediates. For instance, amidation of Et aminocyanoacetate with cyclohexanecarbonyl chloride gave 71% Et cyano[(cyclohexylcarbonyl)amino]acetate, which was methylated using NaOEt and MeI to give 88% Et 2-cyano-2-[(cyclohexylcarbonyl)amino]propanoate. The latter compound was cyclocondensed with 2-methoxybenzamidine HCl to give 21% pyrimidinone intermediate III, which was cyclized by treatment with Me3SiCl and then HMDS to give invention compound IV [R3 = H]. The exptl. inhibition of human PDE 7 (IC50) was 0.34 μM for IV [R3 = H] and 0.055 μM for IV [R3 = 4-methylpiperazin-1-yl]. The invention compds. inhibited PDE 7 with a selectivity of more than 10 times compared to PDE 4.

IT 812667-46-2P, Ethyl cyano[(cyclohexylcarbonyl)amino]acetate
812667-47-3P, Ethyl 2-cyano-2-[(cyclohexylcarbonyl)amino]propanoate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of imidazotriazinone derivs. as selective PDE 7 (phosphodiesterase 7) inhibitors)

RN 812667-46-2 CAPLUS
CN Acetic acid, cyano[(cyclohexylcarbonyl)amino]-, ethyl ester (9CI) (CA INDEX NAME)



RN 812667-47-3 CAPLUS
CN Alanine, 2-cyano-N-(cyclohexylcarbonyl)-, ethyl ester (9CI) (CA INDEX NAME)



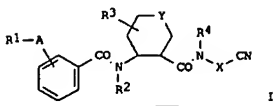
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1059306 CAPLUS
DOCUMENT NUMBER: 142:38025
TITLE: Preparation of benzamide nitrile derivatives for use in pharmaceutical compositions as Cathepsin K inhibitors
INVENTOR(S): Gabriel, Tobias; Krauss, Nancy Elisabeth
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004106285	A1	20041209	WO 2004-EP5830	20040528
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004242865	A1	20041209	AU 2004-242865	20040528
CA 2527632	A1	20041209	CA 2004-2527632	20040528
EP 1633701	A1	20060315	EP 2004-736227	20040528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
BR 2004010929	A	20060627	BR 2004-10929	20040528
CN 1798729	A	20060705	CN 2004-80015394	20040528
JP 2006526586	T	20061124	JP 2006-508225	20040528
US 2004248949	A1	20041209	US 2004-858041	20040601
PRIORITY APPLN. INFO.:			US 2003-475296P P	20030602
			WO 2004-EP5830 W	20040528

OTHER SOURCE(S): MARPAT 142:38025
GI

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



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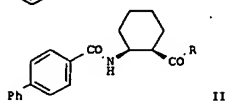

II

AB Benzamides, such as I [R1 = OH, NH2, halogen, alkyl, alkenyl, acyl, heteroaryl, heterocyclyl, alkylsulfonyl, alkylsulfonylamino, etc.; R2, R3, R4 = H, alkyl; A = bond, alkylene, oxaalkylene, azaalkylene, etc.; X = -CH:CH-, -(CRaRb)p-, -O(CRaRb)s-, -NRc(CRaRb)t-, etc; Y = bond, -CH2-, -(CH2)2-; Ra, Rb, Rc = H, alkyl; p, s = 0-3, t = 1-3], were prepared for therapeutic use as in the treatment of diseases or conditions mediated by Cathepsin K, such as osteoporosis, tumor metastasis, instable angina pectoris and/or plaque rupture. Thus, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-1,1'-biphenyl-4-carboxamide II (R = NHCH2CN) was prepared via a series of synthetic steps which included an amidation reaction of Et (1R,2S)-2-aminocyclohexanecarboxylate hydrobromide with 4-biphenylcarboxylic acid to form Et ester II (R = OEt) and, subsequently, an amidation reaction of the corresponding acid II (R = OH) with aminoacetonitrile hydrochloride. The prepared benzamides were assayed for inhibitory activity against Cathepsin K, S, L and B. Pharmaceutical formulations for delivery of these benzamides were disclosed.

IT 805994-04-1P, N-[(1S,2R)-2-[[(Cyanomethyl)amino]carbonyl]cyclohexyl]-1,1'-biphenyl-4-carboxamide 805994-05-2P 805994-06-3P
805994-07-4P 805994-08-5P 805994-09-6P
805994-10-9P 805994-11-0P 805994-12-1P
805994-13-2P 805994-14-3P 805994-15-4P
805994-16-5P 805994-17-6P 805994-18-7P
805994-19-8P 805994-21-2P 805994-22-3P
805994-23-4P 805994-24-5P 805994-25-6P
805994-26-7P 805994-27-8P 805994-28-9P
805994-29-0P 805994-30-3P 805994-31-4P
805994-32-5P 805994-33-6P 805994-34-7P
805994-35-8P 805994-36-9P 805994-37-0P
805994-38-1P 805994-39-2P 805994-40-5P
805994-41-6P 805994-42-7P 805994-43-8P
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805994-47-2P 805994-48-3P 805994-49-4P
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805994-53-0P 805994-54-1P 805994-55-2P
805994-56-3P 805994-57-4P 805994-58-5P
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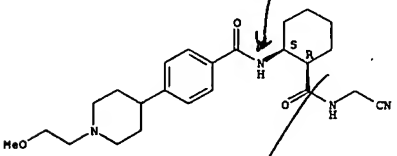
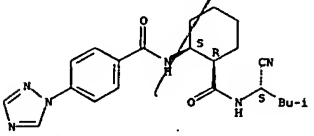
no amide

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



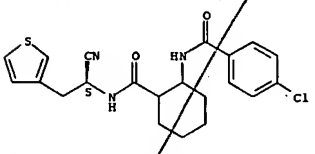
RN 805994-07-4 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(1H-1,2,4-triazol-1-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-08-5 CAPLUS
CN Benzamide, 4-chloro-N-[2-[[[(1S)-1-cyano-2-(3-thienyl)ethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-09-6 CAPLUS
CN Benzamide, N-[2-[[[(1S)-1-cyano-2-(3-thienyl)ethyl]amino]carbonyl]cyclohexyl]-4-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

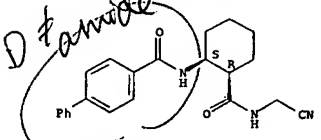
L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

805994-62-1P 805994-63-2P 805994-64-3P
805994-65-4P 805994-66-5P 805994-67-6P
805994-68-7P 805994-69-8P 805994-70-1P
805994-71-2P 805994-72-3P 805994-73-4P
805994-74-5P 805994-75-6P 805994-76-7P
805994-77-8P 805994-78-9P 805994-79-0P
805994-80-3P 805994-81-4P 805994-82-5P
805994-83-6P 805994-84-7P 805994-85-8P
805994-86-9P 805994-87-0P 805994-88-1P
805994-89-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzamide nitrile derivs. for use in pharmaceutical compns. as Cathepsin K inhibitors)

RN 805994-04-1 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

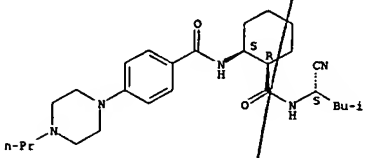
Absolute stereochemistry.

D amide



RN 805994-05-2 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

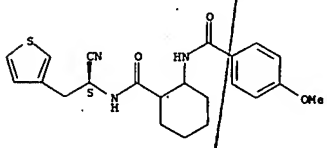
Absolute stereochemistry.



RN 805994-06-3 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[1-(2-methoxyethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

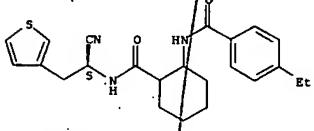
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



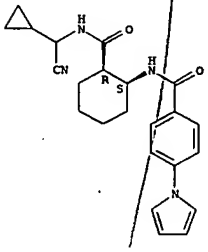
RN 805994-10-9 CAPLUS
CN Benzamide, N-[2-[[[(1S)-1-cyano-2-(3-thienyl)ethyl]amino]carbonyl]cyclohexyl]-4-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-11-0 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carbonyl]cyclohexyl]-4-(1H-pyrrol-1-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

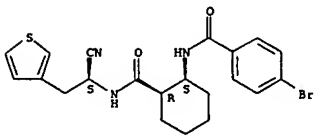


RN 805994-12-1 CAPLUS
CN Benzamide, 4-bromo-N-[(1S,2R)-2-[[[(1S)-1-cyano-2-(3-thienyl)ethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

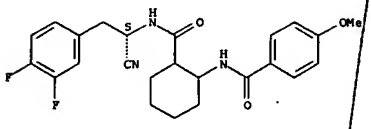
Karen Cheng

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



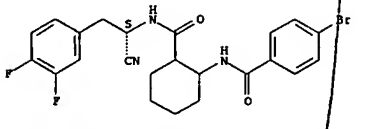
RN 805994-13-2 CAPLUS
CN Benzamide, N-[2-[[[(1S)-1-cyano-2-(3,4-difluorophenyl)ethyl]amino]carbonyl]cyclohexyl]-4-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-14-3 CAPLUS
CN Benzamide, 4-bromo-N-[2-[[[(1S)-1-cyano-2-(3,4-difluorophenyl)ethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

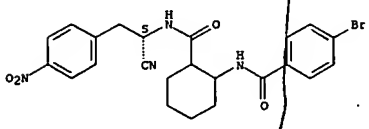
Absolute stereochemistry.



RN 805994-15-4 CAPLUS
CN Benzamide, 4-bromo-N-[2-[[[(1R)-1-cyano-2-(ethylthio)ethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

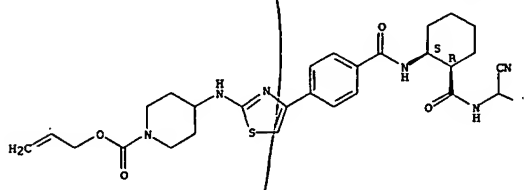
L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 805994-19-8 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[4-[[4-[[[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]amino]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

RN 805994-21-2 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-piperidinylamino)-4-thiazolyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

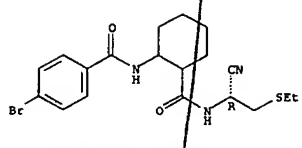
CM 1

CRN 805994-20-1
CMF C27 H34 N6 O2 S

Absolute stereochemistry.

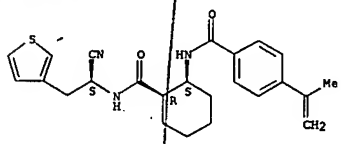
Karen Cheng

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



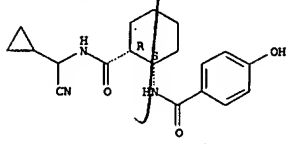
RN 805994-16-5 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-2-(3-thienyl)ethyl]amino]carbonyl]cyclohexyl]-4-(1-methylethenyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-17-6 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carbonyl]cyclohexyl]-4-hydroxy- (9CI) (CA INDEX NAME)

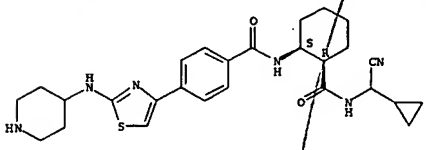
Absolute stereochemistry.



RN 805994-18-7 CAPLUS
CN Benzamide, 4-bromo-N-[2-[[[(1S)-1-cyano-2-(4-nitrophenyl)ethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

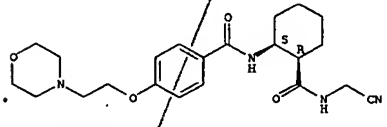


CM 2

CRN 76-05-1
CMF C2 H F3 O2

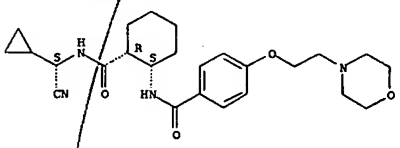
RN 805994-22-3 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinyl)ethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



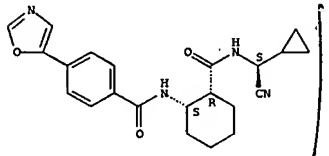
RN 805994-23-4 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(S)-cyanocyclopropylmethyl]amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinyl)ethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



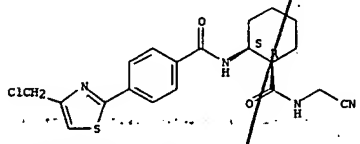
L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 805994-24-5 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(S)-cyanocyclopropylmethyl]amino]carbonyl]cyclohexyl]-4-(5-oxazolyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



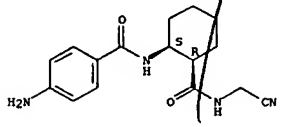
RN 805994-25-6 CAPLUS
CN Benzamide, 4-[4-(chloromethyl)-2-thiazolyl]-N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



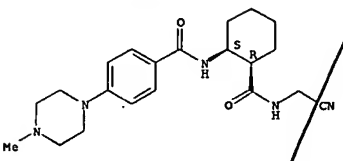
RN 805994-26-7 CAPLUS
CN Benzamide, 4-amino-N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



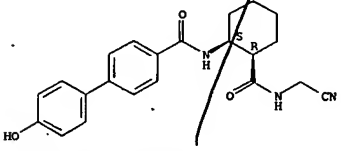
RN 805994-27-8 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



RN 805994-28-9 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4'-hydroxy- (9CI) (CA INDEX NAME)

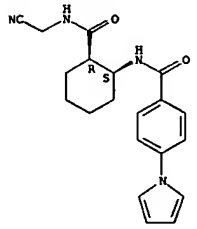
Absolute stereochemistry.



RN 805994-29-0 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1H-pyrrol-1-yl)- (9CI) (CA INDEX NAME)

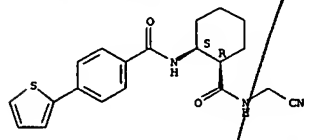
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



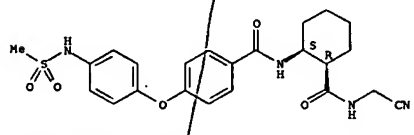
RN 805994-30-3 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(2-thienyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-31-4 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[4-[(methylsulfonyl)amino]phenoxy]- (9CI) (CA INDEX NAME)

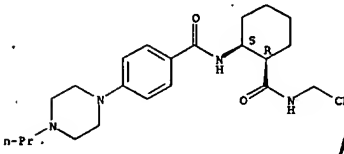
Absolute stereochemistry.



RN 805994-32-5 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

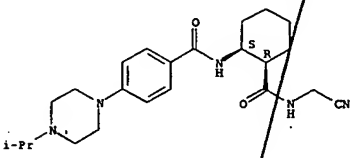
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



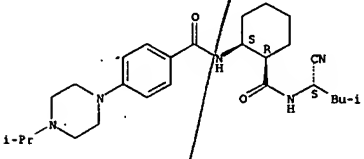
RN 805994-33-6 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[4-(1-methylethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



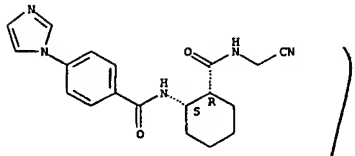
RN 805994-34-7 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[4-(1-methylethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



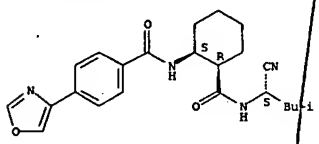
RN 805994-35-8 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1H-imidazol-1-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



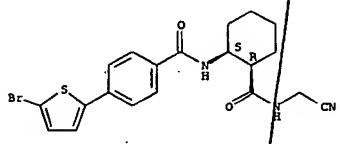
RN 805994-36-9 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(4-oxazolyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-37-0 CAPLUS
CN Benzamide, 4-(5-bromo-2-thienyl)-N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

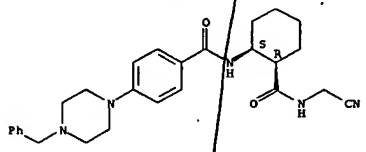
Absolute stereochemistry.



RN 805994-38-1 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

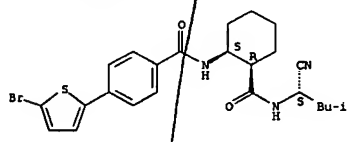
Absolute stereochemistry.

Absolute stereochemistry.



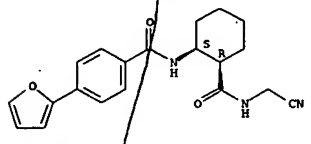
RN 805994-42-7 CAPLUS
CN Benzamide, 4-(5-bromo-2-thienyl)-N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



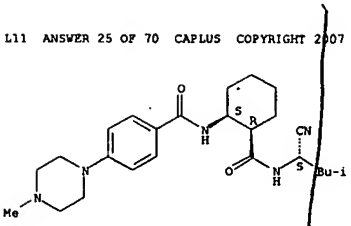
RN 805994-43-8 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(2-furanyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



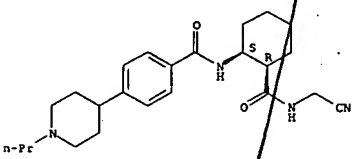
RN 805994-44-9 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



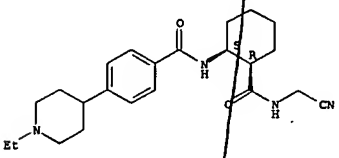
RN 805994-39-2 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-propyl-4-piperidinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

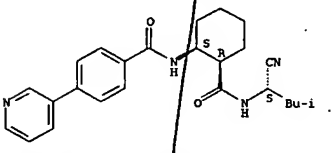


RN 805994-40-5 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-ethyl-4-piperidinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

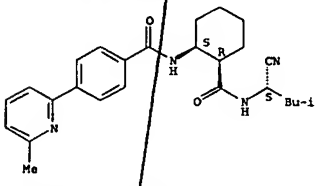


RN 805994-41-6 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[4-(phenylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



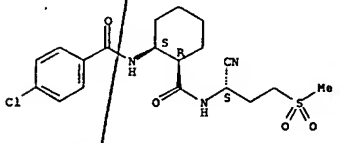
RN 805994-45-0 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(6-methyl-2-pyridinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-46-1 CAPLUS
CN Benzamide, 4-chloro-N-[(1S,2R)-2-[[[(1S)-1-cyano-3-(methylsulfonyl)propyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

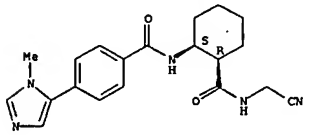
Absolute stereochemistry.



RN 805994-47-2 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-methyl-1H-imidazol-5-yl)- (9CI) (CA INDEX NAME)

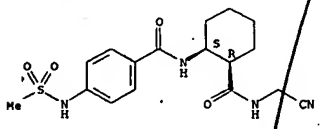
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



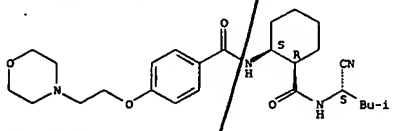
RN 805994-48-3 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-49-4 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinyl)ethoxy]- (9CI) (CA INDEX NAME)

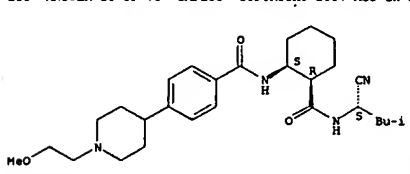
Absolute stereochemistry.



RN 805994-50-7 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-(1-piperidinyl)ethoxy]- (9CI) (CA INDEX NAME)

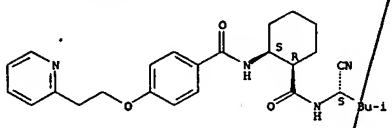
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



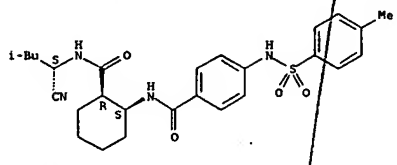
RN 805994-54-1 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-(2-pyridinyl)ethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-55-2 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[[(4-methylphenyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)

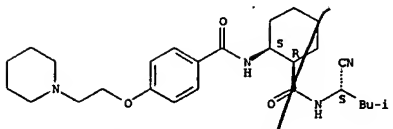
Absolute stereochemistry.



RN 805994-56-3 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[(6-methyl-3-pyridinyl)oxy]- (9CI) (CA INDEX NAME)

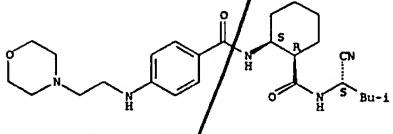
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



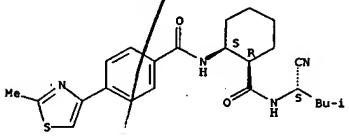
RN 805994-51-8 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[[2-(4-morpholinyl)ethyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-52-9 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(2-methyl-4-thiazolyl)- (9CI) (CA INDEX NAME)

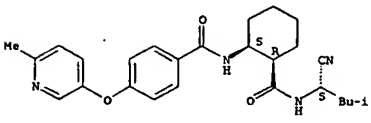
Absolute stereochemistry.



RN 805994-53-0 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[1-(2-methoxyethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

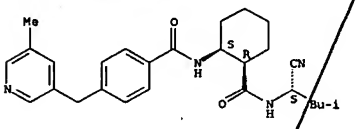
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



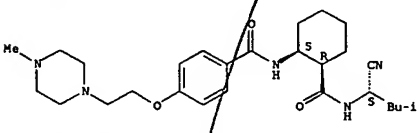
RN 805994-57-4 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[(5-methyl-3-pyridinyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



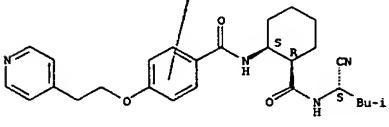
RN 805994-58-5 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)ethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



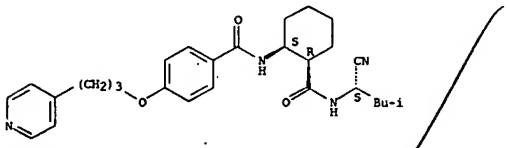
RN 805994-59-6 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-(4-pyridinyl)ethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



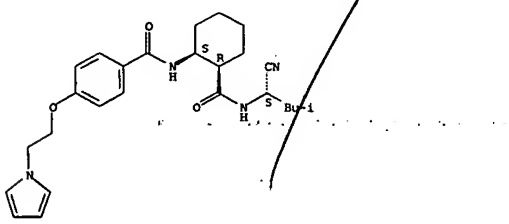
L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 805994-60-9 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[3-(4-pyridinyl)propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-61-0 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-(1H-pyrrol-1-yl)ethoxy]- (9CI) (CA INDEX NAME)

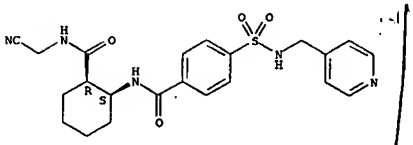
Absolute stereochemistry.



RN 805994-62-1 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[[(4-pyridinylmethyl)amino]sulfonyl]- (9CI) (CA INDEX NAME)

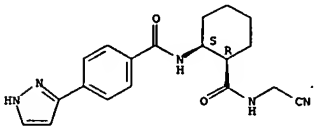
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



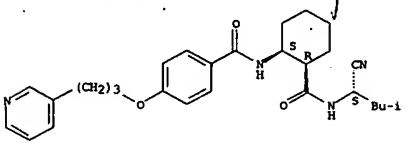
RN 805994-63-2 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-64-3 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[3-(3-pyridinyl)propoxy]- (9CI) (CA INDEX NAME)

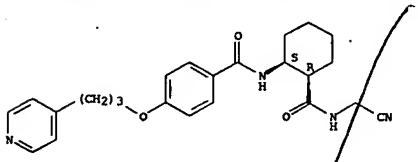
Absolute stereochemistry.



RN 805994-65-4 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[3-(4-pyridinyl)propoxy]- (9CI) (CA INDEX NAME)

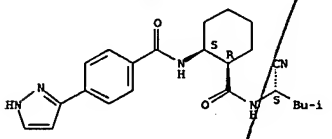
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



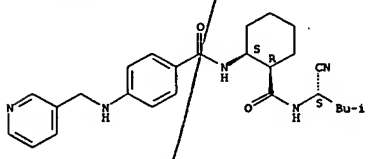
RN 805994-66-5 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-67-6 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[(3-pyridinylmethyl)amino]- (9CI) (CA INDEX NAME)

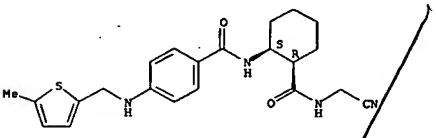
Absolute stereochemistry.



RN 805994-68-7 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[[(5-methyl-2-thienyl)methyl]amino]- (9CI) (CA INDEX NAME)

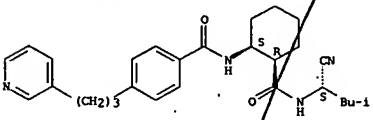
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



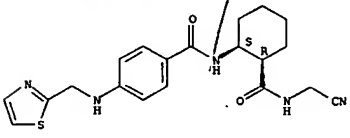
RN 805994-69-8 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[3-(3-pyridinyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-70-1 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[(2-thiazolylmethyl)amino]- (9CI) (CA INDEX NAME)

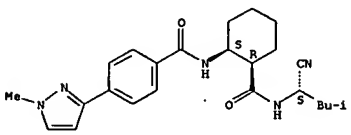
Absolute stereochemistry.



RN 805994-71-2 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(1-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)

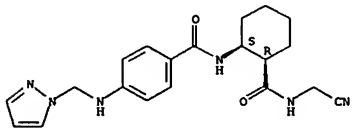
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



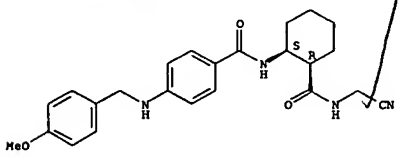
RN 805994-72-3 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[(1H-pyrazol-1-ylmethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-73-4 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[[(4-methoxyphenyl)methyl]amino]- (9CI) (CA INDEX NAME)

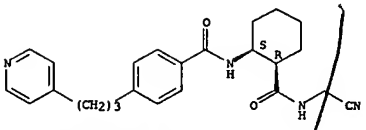
Absolute stereochemistry.



RN 805994-74-5 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[3-(4-pyridinyl)propyl]- (9CI) (CA INDEX NAME)

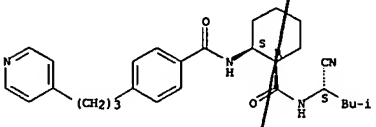
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



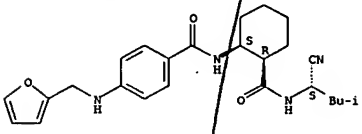
RN 805994-75-6 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[3-(4-pyridinyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-76-7 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[(2-furanylmethyl)amino]- (9CI) (CA INDEX NAME)

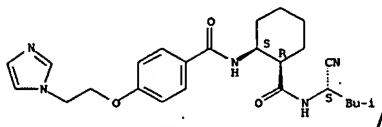
Absolute stereochemistry.



RN 805994-77-8 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-(1H-imidazol-1-yl)ethoxy]- (9CI) (CA INDEX NAME)

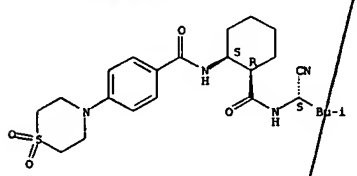
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



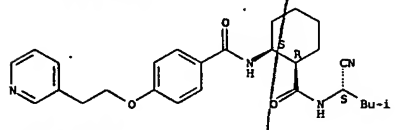
RN 805994-78-9 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(1,1-dioxido-4-thiomorpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-79-0 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-(3-pyridinyl)ethoxy]- (9CI) (CA INDEX NAME)

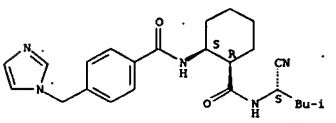
Absolute stereochemistry.



RN 805994-80-3 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(1H-imidazol-1-ylmethyl)- (9CI) (CA INDEX NAME)

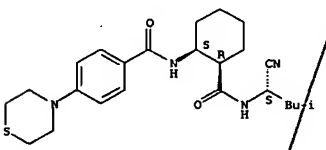
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



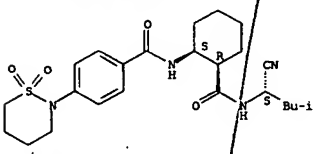
RN 805994-81-4 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(4-thiomorpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-82-5 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(tetrahydro-1,1-dioxido-2H-1,2-thiazin-2-yl)- (9CI) (CA INDEX NAME)

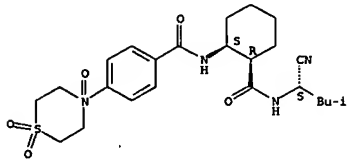
Absolute stereochemistry.



RN 805994-83-6 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(1,1,4-trioxido-4-thiomorpholinyl)- (9CI) (CA INDEX NAME)

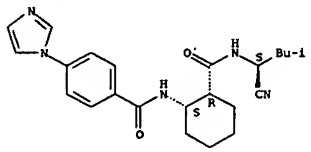
Absolute stereochemistry.

L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



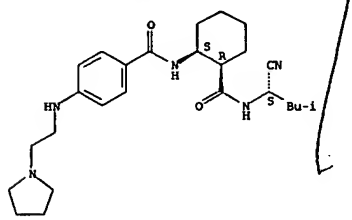
RN 805994-84-7 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(1H-imidazol-1-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-85-8 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[[2-(1-pyrrolidinyl)ethyl]amino]- (9CI) (CA INDEX NAME)

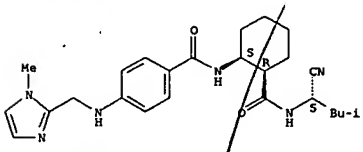
Absolute stereochemistry.



L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

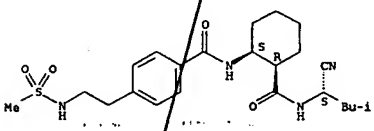
RN 805994-86-9 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[[(1-methyl-1H-imidazol-2-yl)methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



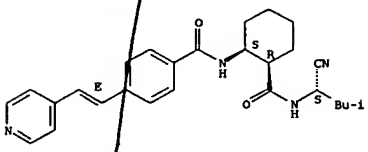
RN 805994-87-0 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-[(methylsulfonyl)amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



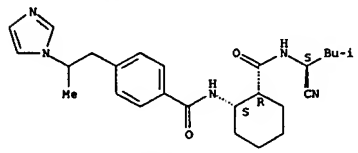
RN 805994-88-1 CAPLUS
CN Benzamide, N-[(1R,2S)-2-[[[(1R)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[(1E)-2-(4-pyridinyl)ethenyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 805994-89-2 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-[2-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)

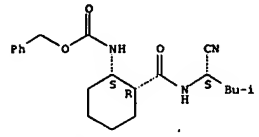
Absolute stereochemistry.



IT 541522-77-4P 680568-92-7P 680568-93-8P
680569-68-0P 805994-95-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzamide nitrile derivs. for use in pharmaceutical compns.
as Cathepsin K inhibitors)

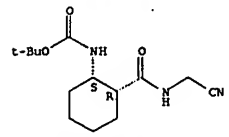
RN 541522-77-4 CAPLUS
CN Carbamic acid, [(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 680568-92-7 CAPLUS
CN Carbamic acid, [(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

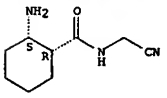
Absolute stereochemistry.



RN 680568-93-8 CAPLUS
CN Cyclohexanecarboxamide, 2-amino-N-(cyanomethyl)-, (1R,2S)- (9CI) (CA

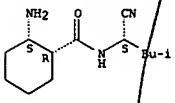
L11 ANSWER 25 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
INDEX NAME)

Absolute stereochemistry.



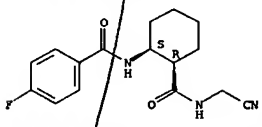
RN 680569-68-0 CAPLUS
CN Cyclohexanecarboxamide, 2-amino-N-[(1S)-1-cyano-3-methylbutyl]-, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 805994-95-0 CAPLUS
CN Benzamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

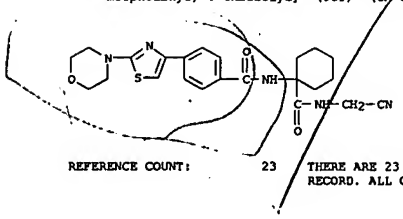
Karen Cheng

L11 ANSWER 26 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:1006910 CAPLUS
DOCUMENT NUMBER: 142:129533
TITLE: An activity-based probe for the determination of cysteine cathepsin protease activities in whole cells
AUTHOR(S): Falgueyret, Jean-Pierre; Black, W. Cameron; Cromlish, Wanda; Desmarais, Sylvie; Lamontagne, Sonia; Mellon, Christophe; Riendeau, Denis; Rodan, Sevgi; Tawa, Paul; Wesolowski, Gregg; Bass, Kathryn E.; Venkatraman, Shankar; Percival, M. David
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, Can.
SOURCE: Analytical Biochemistry (2004), 335(2), 218-227
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors describe a novel diazomethylketone-containing irreversible inhibitor (BIL-DMK) which is specific for a subset of pharmaceutically important cysteine cathepsin proteases. BIL-DMK rapidly inactivates cathepsins B, F, K, L, S, and V in isolated enzyme assays and labels cathepsins in whole cells. The presence of catalytically active cathepsins B, L, and K or S was demonstrated using radioiodinated BIL-DMK in HepG2 (hepatoma), HIG82 (rabbit synoviocyte), and Ramos (B lymphoma) cell lines, resp. The identity of each protein labeled was confirmed from the isoelec. point and mol. mass of the radioactive spots on two-dimensional gel and by comigration with each cathepsin as identified by immunoblotting. These cell lines were used to establish whole-cell enzyme occupancy assays to determine the potency of both irreversible and reversible inhibitors against each cathepsin in their native cellular lysosomal or endosomal environment. These whole-cell enzyme occupancy assays are useful to determine the cellular permeability of competing inhibitors and have the advantage of not requiring specific substrates for each cathepsin of interest.

IT 294622-81-4
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; diazomethylketone-containing irreversible inhibitor preparation as activity-based probe for determination of cathepsin in whole cells)
RN 294622-81-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

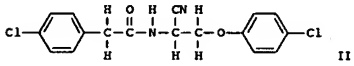
L11 ANSWER 26 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L11 ANSWER 27 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:650899 CAPLUS
DOCUMENT NUMBER: 141:173978
TITLE: Preparation of aminoacetonitrile derivatives as agricultural and horticultural insecticides
INVENTOR(S): Andoh, Nobuharu; Sanpei, Osamu; Sakata, Kazuyuki
PATENT ASSIGNEE(S): Nihon Nohyaku Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 48 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1445251	A1	20040811	EP 2004-10346	19990428
EP 1445251	B1	20061227		
R: CH, DE, FR, GB, IT, LI				
EP 953565	A2	19991103	EP 1999-107461	19990428
EP 953565	A3	20021204		
EP 953565	B1	20040908		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: JP 1998-137806 A 19980501
EP 1999-107461 A3 19990428
OTHER SOURCE(S): MARPAT 141:173978
GI

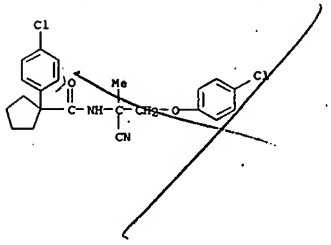


II

AB The title compds. Ar1(Q)dC(O)NR3C(CN)R4(CR5R6)aW(CR7R8)bAr2 [I; Ar1, Ar2 = (substituted) Ph, (substituted) phenyloxy, (substituted) phenylacetylene; (substituted) pyridyl and (substituted) naphthyl; Q = CR1R2 (wherein R1, R2 = H, halo, (halo)alkyl, etc.); R3 = H, (halo)alkyl, etc.; R4-R8 = H, halo, (halo)alkyl, etc.; W = O, S, SO2 or NR9 (wherein R9 = H, alkyl); a, b = 0-4; d = 0-1], useful as insecticides, were prepared E.g., a multi-step synthesis of II (starting from 4-chlorophenol and bromoacetaldehyde dimethylacetal), was given. The compds. I were tested against diamondback moth and against smaller tea tortrix (data were given for representative compds. I).

IT 247198-01-2P
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of aminoacetonitrile derivs. as agricultural and horticultural insecticides)
RN 247198-01-2 CAPLUS
CN Cyclopentanecarboxamide, N-[2-(4-chlorophenoxy)-1-cyano-1-methylethyl]-1-(4-chlorophenyl)- (9CI) (CA INDEX NAME)

L11 ANSWER 27 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



Karen Cheng

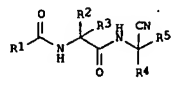
10560672restrict

L11 ANSWER 28 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:515539 CAPLUS
DOCUMENT NUMBER: 141:71829
TITLE: Cyanomethyl derivatives as cysteine protease inhibitors
INVENTOR(S): Graupe, Michael; Lau, Agnes J.; Link, John O.; Liu, Yang; Mossman, Craig J.; Patterson, John W.; Zipfel, Sheila M.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052921	A1	20040624	WO 2003-US37979	20031126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506114	A1	20040624	CA 2003-2506114	20031126
AU 2003298740	A1	20040630	AU 2003-298740	20031126
EP 1569954	A1	20050907	EP 2003-796499	20031126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006122184	A1	20060608	US 2005-536889	20051017
PRIORITY APPLN. INFO.:			US 2002-431354P P	20021205
			WO 2003-US37979 W	20031126

OTHER SOURCE(S): MARPAT 141:71829
GI

L11 ANSWER 28 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



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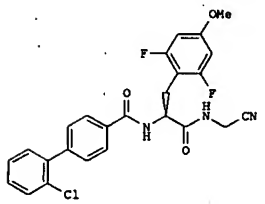
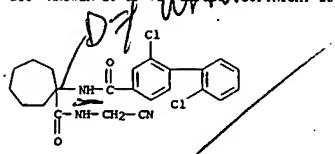


II

AB The dipeptide derivs. [I [R1 = substituted Ph, aryl, diaryl, heterodiaryl, furanyl, arylfuranyl, pyrazolyl, etc.; R2 = H, (un)substituted cycloalkyl, indolyl, alkylindolyl, Me, Et, Pr, pentyl, etc.; R3 = H, or R2 and R3 together with the carbon atom to which they are attached formed (un)substituted cycloalkylene, cycloalkenylene or spirocycloalkylene; R4 = H; R5 = H, (un)substituted alkyl or heteroaryl, or R4 and R5 together with the carbon atom to which they are attached form cycloalkylene or heterocycloalkylene]] were prepared as cysteine protease inhibitors, in particular, cathepsins B, K, L, F, and S, for treating diseases mediated by these proteases. Thus, compound II was prepared via peptide coupling of 2'-chlorobiphenyl-4-carboxylic acid with synthesized 2(S)-amino-N-cyanomethyl-3-(2,6-difluoro-4-methoxyphenyl)-propionamide. Compds. of the invention were tested by in vitro essays for protease activity and showed cathepsins B, K, L, F, and S inhibitory activity.
IT 710350-02-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dipeptide cyanomethyl derivs. as cysteine protease inhibitors)
RN 710350-02-0 CAPLUS
CN Cycloheptanecarboxamide, N-(cyanomethyl)-1-[[(2,2'-dichloro[1,1'-biphenyl]-4-yl)carbonyl]amino]- (9CI) (CA INDEX NAME)

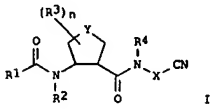
L11 ANSWER 28 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L11 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:331784 CAPLUS
DOCUMENT NUMBER: 140:339193
TITLE: Preparation of indole nitriles as cysteine protease, in particular Cathepsin K inhibitors
INVENTOR(S): Bamberg, Joe Timothy; Gabriel, Tobias; Krauss, Nancy Elisabeth; Mirzadegan, Taraneh; Palmer, Wylie Solang; Smith, David Bernard
PATENT ASSIGNEE(S): Roche Palo Alto, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 141 pp., Cont.-in-part of U.S. Ser. No. 308,963.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004077646	A1	20040422	US 2003-453112	20030602
US 6759428	B2	20040706		
US 2003212097	A1	20031113	US 2002-308963	20021203
US 6747053	B2	20040608		
PRIORITY APPLN. INFO.:			US 2001-336750P P	20011204
			US 2002-308963 A2	20021203

OTHER SOURCE(S): MARPAT 140:339193
GI



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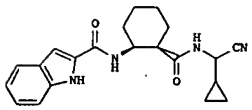

II

AB Title compds. I [wherein n = 0-2; R1 = (un)substituted indolyl, indazolyl, benzothiazolyl, indolizinyl, tetrahydropyridoindolyl; benzopyrrolothiazolyl; X = [CH(R5R6)]q; q = 1-2; R2, R3, R4, R5 =

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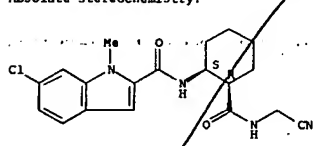
L11 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
independently H, alkyl; R6 = H, cyclo/alkyl, (CRaRb)oA; Ra, Rb = independently H, alkyl; o = 0-4; A = OH and derivs., (un)substituted Ph, pyridyl, imidazolyl, morpholinyl, CO2H and derivs., etc.; Y =(CH2)m; m = 1-3; their pharmaceutically acceptable salts, solvates and prodrugs] were prepd. as cysteine protease, in particular Cathepsin K inhibitors. The compds. are useful for the treatment of diseases which are assocd. with cysteine proteases such as osteoporosis, tumor metastasis, unstable angina pectoris and/or plaque rupture. Thus, Et (1R,2S)-2-aminocyclohexanecarboxylate-HBr was treated with indole-2-carboxylic acid, followed by ester hydrolysis and amidation with (R,S)-amino(cyclopropyl)acetonitrile to give the amide II. I selectively inhibited Cathepsin K (no data).

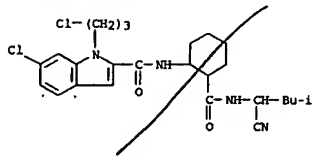
IT 680568-91-6P, 6-Chloro-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680568-95-0P 680569-80-6P, 6-Chloro-1-(3-hydroxypropyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680569-82-8P, 6-Chloro-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylsulfanylpropyl)carbamoyl]cyclohexyl]amide 680569-84-0P 680570-08-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(Cathepsin K inhibitor; preparation of indole nitriles as cysteine protease,
in particular Cathepsin K inhibitors)

RN 680568-91-6 CAPLUS
CN 1H-Indole-2-carboxamide, 6-chloro-N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

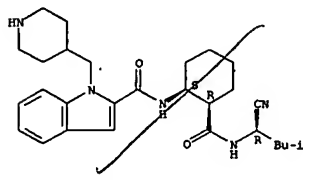


RN 680568-95-0 CAPLUS
CN 1H-Indole-2-carboxamide, 6-chloro-1-(3-chloropropyl)-N-[2-[[(1-cyano-3-methylbutyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)



L11 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.



● HCl

IT 680568-80-3P 680568-81-4P 680568-82-5P, 6-Chloro-1-[2-(morpholin-4-yl)ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-cyano(cyclopropyl)methyl]carbamoyl]cyclohexyl]amide 680568-83-6P, 6-Chloro-1-(2-dimethylaminoethyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-cyano(cyclopropyl)methyl]carbamoyl]cyclohexyl]amide 680568-84-7P, 6-Chloro-1-(3-dimethylaminopropyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-cyano(cyclopropyl)methyl]carbamoyl]cyclohexyl]amide 680568-85-8P, 1-[3-(Morpholin-4-yl)propyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-cyano(cyclopropyl)methyl]carbamoyl]cyclohexyl]amide 680568-86-9P, 3-(3-Dimethylaminopropyl)-1H-indazole-5-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680568-89-2P, 1-Methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cycloheptyl]amide 680568-97-2P 680568-98-3P 680568-99-4P 680569-01-1P 680569-03-3P 680569-04-4P 680569-05-5P 680569-06-6P, 1-[2-[(Piperidin-1-ylsulfonyl)amino]ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680569-09-9P 680569-10-2P 680569-12-4P 680569-14-6P, 6-Bromo-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680569-23-7P, 1-Methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-[4-(2-methoxyethyl)piperazin-1-yl]propyl]carbamoyl]cyclohexyl]amide 680569-25-9P, 1-Methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-4-(morpholin-4-yl)-4-oxobutyl]carbamoyl]cyclohexyl]amide 680569-28-2P 680569-31-7P 680569-32-8P 680569-34-0P 680569-38-4P, 1-Methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-(methanesulfonyl)propyl]carbamoyl]cyclohexyl]amide 680569-40-8P 680569-45-3P 680569-46-4P 680569-51-1P 680569-53-3P 680569-54-4P 680569-59-9P 680569-60-2P 680569-63-5P, 1-(3-Hydroxypropyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680569-64-6P, 1-[2-(2-Hydroxyethoxy)ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680569-70-4P, 1-[2-(2-Methoxyethoxy)ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide

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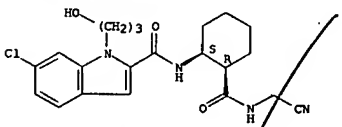
L11 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

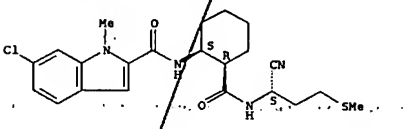
RN 680569-80-6 CAPLUS
CN 1H-Indole-2-carboxamide, 6-chloro-N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-1-(3-hydroxypropyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



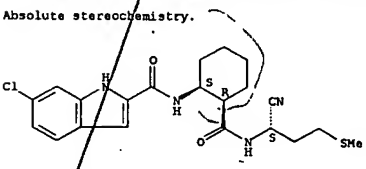
RN 680569-82-8 CAPLUS
CN 1H-Indole-2-carboxamide, 6-chloro-N-[(1S,2R)-2-[[[(1S)-1-cyano-3-(methylthio)propyl]amino]carbonyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 680569-84-0 CAPLUS
CN 1H-Indole-2-carboxamide, 6-chloro-N-[(1S,2R)-2-[[[(1S)-1-cyano-3-(methylthio)propyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 680570-08-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[[(1R)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-1-(4-piperidinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

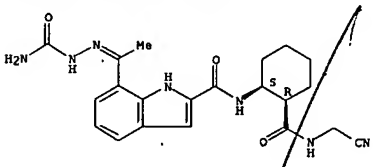
L11 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
680569-73-7P, 1-[3-(Piperidin-1-yl)propyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680569-76-0P, 6-Chloro-1-(2-hydroxyethyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680569-78-2P, 6-Chloro-1-[2-(morpholin-4-yl)ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680569-79-3P, 6-Chloro-1-[3-(piperidin-1-yl)propyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680569-85-1P, 6-Chloro-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-(methanesulfonyl)propyl]carbamoyl]cyclohexyl]amide 680569-86-2P, 6-Chloro-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-(methanesulfonyl)propyl]carbamoyl]cyclohexyl]amide 680569-87-3P 680569-90-8P, 6-Chloro-1-[3-(methanesulfonyl)propyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680569-91-9P 680569-95-3P, 1-(2-Hydroxy-2-methylpropyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680569-98-6P, 1-[2-(2-Hydroxyethylamino)ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-00-7P 680570-02-9P 680570-04-1P 680570-05-2P 680570-06-3P 680570-07-4P 680570-11-0P 680570-12-1P 680570-13-2P, 1-[1-(2-Methoxyethyl)piperidin-4-ylmethyl]-1H-indole-2-carboxylic acid [2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680570-14-3P 680570-15-4P 680570-19-8P 680570-20-1P 680570-21-2P 680570-22-3P 680570-23-4P, 6-Fluoro-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-cyano(cyclopropyl)methyl]carbamoyl]cyclohexyl]amide 680570-24-5P, 5-Fluoro-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylsulfanylpropyl)carbamoyl]cyclohexyl]amide 680570-25-6P, 1-[3-(Morpholin-4-yl)propyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-26-7P 680570-27-8P, 1-(2-Hydroxyethyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-cyano(cyclopropyl)methyl]carbamoyl]cyclohexyl]amide 680570-28-9P 680570-29-0P, 1-(2-Dimethylaminoethyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-30-3P, 1-[2-(Morpholin-4-yl)ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-31-4P 680570-32-5P, 6-Bromo-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-33-6P, 6-Bromo-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-34-7P, 1-(3-Hydroxy-2-hydroxymethylpropyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-35-8P, 1-(3-Hydroxy-3-methylbutyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-36-9P, 1-(3-Dimethylaminopropyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-37-0P, 6-Bromo-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680570-38-1P, 1-[2-(Methanesulfonyl)ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-39-2P, 6-Chloro-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-40-5P, 1-(1-Methylpiperidin-4-ylmethyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-methylbutyl]carbamoyl]cyclohexyl]amide 680570-41-6P, 1-[1-(2-Methoxyethyl)piperidin-4-ylmethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[((S)-1-cyano-3-

L11 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
methylbutyl)carbamoyl]cyclohexyl]amide 680570-42-7P,
1-Methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-(4-methylpiperazin-1-yl)propyl]carbamoyl]cyclohexyl]amide
680570-43-8P, 5-Fluoro-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-(methanesulfonyl)propyl]carbamoyl]cyclohexyl]amide 680570-44-9P, 6-Chloro-1-[2-(morpholin-4-yl)ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl]carbamoyl]cyclohexyl]amide 680570-45-0P,
1-[3-[1-(2-Methoxyethyl)piperidin-4-yl]propyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl]carbamoyl]cyclohexyl]amide
680570-46-1P, 6-(Pyridin-3-yl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl]carbamoyl]cyclohexyl]amide
680570-47-2P, 1-[2-[1-(2-Methoxyethyl)piperidin-4-yl]ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl]carbamoyl]cyclohexyl]amide 680570-48-3P,
1-[2-(1-Methylpiperidin-4-yl)ethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl]carbamoyl]cyclohexyl]amide
680570-49-4P 680570-50-7P, 6-[2-(Methanesulfonyl)ethyl]-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl]carbamoyl]cyclohexyl]amide 680570-51-8P
680570-52-9P, 6-(4-Methylpiperazin-1-ylmethyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide
680570-53-0P, 6-[(Pyrazol-1-yl)methyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680570-54-1P
, 6-(Imidazol-1-yl)methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680570-55-2P,
1-Methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-2-(1-methyl-1H-imidazol-4-yl)ethyl]carbamoyl]cyclohexyl]amide
680570-56-3P, 6-Chloro-1-(3-dimethylaminopropyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl]carbamoyl]cyclohexyl]amide 680570-57-4P, 6-Chloro-1-(2-dimethylaminoethyl)-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl]carbamoyl]cyclohexyl]amide 680570-58-5P,
1-Methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-(cyclopropylcarbamoyl)propyl]carbamoyl]cyclohexyl]amide
680570-59-6P, 1-Methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-dimethylaminopropyl)carbamoyl]cyclohexyl]amide 680570-61-0P, 1-[1-(2-Methoxyethyl)piperidin-4-ylmethyl]-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680570-62-1P 680570-63-2P 680570-64-3P,
1-[3-(Morpholin-4-yl)propyl]-1H-indole-5-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide
680570-65-4P, 1-(2-Dimethylaminoethyl)-1H-indole-5-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide
680570-66-5P, 1-(3-Dimethylaminopropyl)-1H-indole-5-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide
680570-67-6P, 6-Methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680570-68-7P
, 6-(3-Hydroxy-3-methylbutyl)-1-methyl-1H-indole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide
680570-69-8P 680570-70-1P, 1H-Indole-5-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680570-71-2P
, 5-(6-Methylpyridin-2-yl)thiophene-2-carboxylic acid N-[(1S,2R)-2-(N-cyanomethylcarbamoyl)cyclohexyl]amide 680570-72-3P,
Benzo[d]pyrrolo[2,1-b]thiazole-2-carboxylic acid N-[(1S,2R)-2-[[(S)-1-

L11 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-73-4P,
1H-Indole-5-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide 680570-74-5P,
1H-Indole-6-carboxylic acid N-[(1S,2R)-2-[[(S)-1-cyano-3-methylbutyl)carbamoyl]cyclohexyl]amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Cathepsin K inhibitor; prepn. of indole nitriles as cysteine protease, in particular Cathepsin K inhibitors)

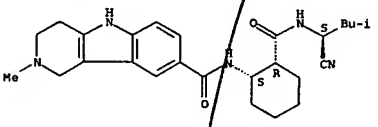
RN 680568-80-3 CAPLUS
CN 1H-Indole-2-carboxamide, 7-[1-[(aminocarbonyl)hydrazono]ethyl]-N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 680568-81-4 CAPLUS
CN 1H-Pyrido[4,3-b]indole-8-carboxamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-2,3,4,5-tetrahydro-2-methyl- (9CI) (CA INDEX NAME)

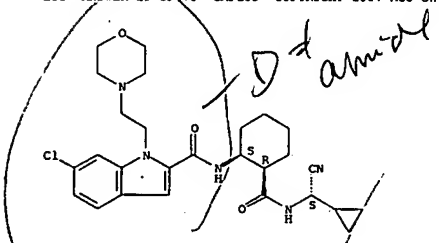
Absolute stereochemistry.



RN 680568-82-5 CAPLUS
CN 1H-Indole-2-carboxamide, 6-chloro-N-[(1S,2R)-2-[[[(S)-cyanocyclopropylmethyl]amino]carbonyl]cyclohexyl]-1-[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)

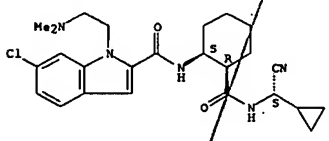
Absolute stereochemistry.

L11 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



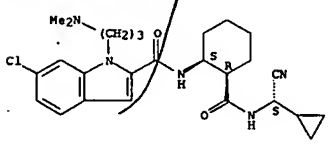
RN 680568-83-6 CAPLUS
CN 1H-Indole-2-carboxamide, 6-chloro-N-[(1S,2R)-2-[[[(S)-cyanocyclopropylmethyl]amino]carbonyl]cyclohexyl]-1-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 680568-84-7 CAPLUS
CN 1H-Indole-2-carboxamide, 6-chloro-N-[(1S,2R)-2-[[[(S)-cyanocyclopropylmethyl]amino]carbonyl]cyclohexyl]-1-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

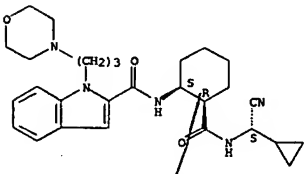


RN 680568-85-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[[(S)-cyanocyclopropylmethyl]amino]carbonyl]cyclohexyl]-1-[3-(4-morpholinyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

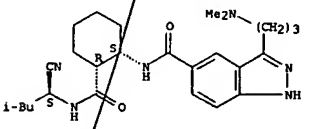
Karen Cheng

L11 ANSWER 29 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



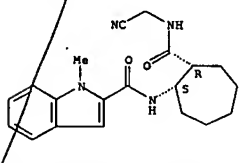
RN 680568-86-9 CAPLUS
CN 1H-Indazole-5-carboxamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-3-[3-(dimethylamino)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 680568-89-2 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cycloheptyl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



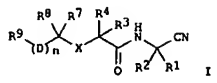
RN 680568-97-2 CAPLUS
CN 1H-Indole-2-carboxamide, 6-chloro-N-[2-[[(1-cyano-3-methylbutyl)amino]carbonyl]cyclohexyl]-1-[2-(dimethylamino)ethyl]- (9CI) (CA INDEX NAME)

L11 ANSWER 30 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:220304 CAPLUS
DOCUMENT NUMBER: 140:270877
TITLE: Preparation of heterocyclic-substituted amides as cathepsin cysteine protease inhibitors
INVENTOR(S): Boyd, Michael; Gagnon, Marc; Lau, Cheuk; Mellon, Christophe; Scheigetz, John
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

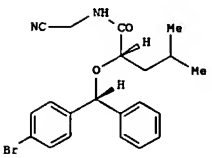
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022526	A1	20040318	WO 2003-CA1346	20030903
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2495939	A1	20040318	CA 2003-2495939	20030903
AU 2003266052	A1	20040329	AU 2003-266052	20030903
EP 1537074	A1	20050608	EP 2003-793540	20030903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005537326	T	20051208	JP 2004-533125	20030903
US 2006122268	A1	20060608	US 2005-525264	20050222
PRIORITY APPLN. INFO.:			US 2002-408064P P	20020904
			WO 2003-CA1346 W	20030903

OTHER SOURCE(S): MARPAT 140:270877
GI

L11 ANSWER 30 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



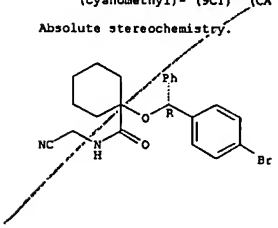
I



II

AB Title compds. I [R1-4 = H, alkyl, alkenyl,etc.; X = O, S, SO2, alkyl; R7-8 = H, alk(en/yn)yl, haloalkyl, alkoxy, NO2, CN, etc.; D = (hetero)aryl, cycloalkyl, etc.; R9 = H, OH, CN, alkyl, etc.; n = 0-3] are prepared For instance, (5S)-2-(4-bromophenyl)-5-isobutyl-1,3-dioxolan-4-one (preparation given) is reacted with PhMgBr (Et2O, ZnCl2, -40°) and the resulting carboxylic acid coupled to aminoacetonitrile (DMF, HATU, Et3N) to give II. I are cysteine protease inhibitors, including but not limited to, inhibitors of cathepsins K, L, S and B and are useful for treating diseases in which inhibition of bone resorption is indicated, such as osteoporosis. They have the following structure: Formula (I).
IT 672328-32-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic-substituted amides as cathepsin cysteine protease inhibitors)
RN 672328-32-4 CAPLUS
CN Cyclohexanecarboxamide, 1-[(R)-(4-bromophenyl)phenylmethoxy]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

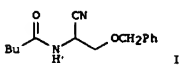
Absolute stereochemistry.



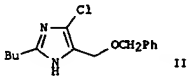
L11 ANSWER 30 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 31 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:141907 CAPLUS
DOCUMENT NUMBER: 140:339247
TITLE: New Method for the Synthesis of Diversely Functionalized Imidazoles from N-Acylated α-Aminonitriles
AUTHOR(S): Zhong, Yong-Li; Lee, Jaemoon; Reamer, Robert A.; Askin, David
CORPORATE SOURCE: Department of Process Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
SOURCE: Organic Letters (2004), 6(6), 929-931
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:339247
GI



I

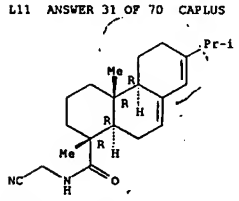


II

AB A new general method for the synthesis of medicinally important diversely functionalized imidazoles from N-acylated α-aminonitriles has been developed. N-Acylated α-aminonitriles were reacted with triphenylphosphine and carbon tetrahalide to afford 2,4-disubstituted 5-halo-1H-imidazoles in good yield. This new methodol. was applied for the synthesis of 2-butyl-4-chloro-5-hydroxymethylimidazole. These haloimidazoles can be directly converted to 2,4,5-trisubstituted imidazoles through palladium-catalyzed coupling reactions. The reaction of N-[1-cyano-2-(phenylmethoxy)ethyl]pentanamide (I) with carbon tetrachloride gave 2-butyl-4-chloro-5-[(phenylmethoxy)methyl]-1H-imidazole (II) which upon deprotection gave 2-butyl-5-chloro-1H-imidazole-4-methanol, a synthetic intermediate for cozaar.
IT 679412-59-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of functionalized imidazoles by triphenylphosphine-mediated reaction of halomethanes with N-(cyanomethyl) amides)
RN 679412-59-0 CAPLUS
CN 1-Phenanthrenecarboxamide, N-(cyanomethyl)-1,2,3,4,4a,4b,5,6,10,10a-decahydro-1,4a-dimethyl-7-(1-methylethyl)-, (1R,4aR,4bR,10aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L11 ANSWER 31 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

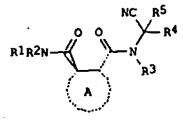
L11 ANSWER 32 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:2871 CAPLUS
DOCUMENT NUMBER: 140:77162
TITLE: Preparation of cyclohexane dicarboxamides for treating diseases associated with cysteine protease activity
INVENTOR(S): Bailey, Andrew; Pairaudeau, Garry; Patel, Anil; Thom, Stephen
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000825	A1	20031231	WO 2003-SE1080	20030623
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003243097	A1	20040106	AU 2003-243097	20030623
EP 1532124	A1	20050525	EP 2003-761003	20030623
EP 1532124	B1	20060719		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005533805	T	20051110	JP 2004-515330	20030623
AT 333451	T	20060815	AT 2003-761003	20030623
US 2005245522	A1	20051103	US 2004-518818	20041220

PRIORITY APPLN. INFO.: SE 2002-1977 A 20020624
WO 2003-SE1080 W 20030623

OTHER SOURCE(S): MARPAT 140:77162
GI



I

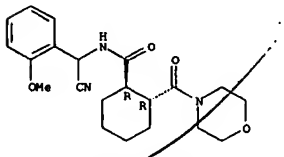
AB The title compds. [I; A = 6-membered ring optionally containing a double bond
and optionally containing an oxygen atom or NR group in the ring; R = H,

L11 ANSWER 32 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
alkyl; R1, R2 = alkyl, cycloalkyl both of which can optionally contain one or more O, S or (un)substituted NH; or NR1R2 = 3,4-dihydroisoquinoline, 5-6 membered satd. ring optionally contg. a further O, S or N atom, etc.; R3, R4 = H, alkyl; R5 = H, alkyl, cycloalkyl, etc.; or R4 and R5 together form a 5-6 membered satd. ring optionally contg. a further O, S, (un)substituted NH], useful for treating diseases assocd. with cysteine protease activity such as pain, were prepd. E.g., a 2-step synthesis of (1R,2R)-N-[cyano(2-methoxyphenyl)methyl]-2-(morpholin-4-ylcarbonyl)cyclohexanecarboxamide, was given. The compds. I are reversible inhibitors of cysteine proteases S, K, F, L and B. Of particular interest are diseases assocd. with Cathepsin S (no data). Pharmaceutical compn. comprising the compd. I is claimed.

IT 639792-00-0P 639792-01-1P 639792-02-2P
639792-03-3P 639792-04-4P 639792-05-5P
639792-06-6P 639792-07-7P 639792-08-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclohexane dicarboxamides for treating diseases associated
with cysteine protease activity)

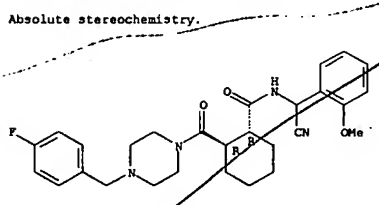
RN 639792-00-0 CAPLUS
CN Cyclohexanecarboxamide, N-[cyano(2-methoxyphenyl)methyl]-2-(4-morpholinylcarbonyl)-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 639792-01-1 CAPLUS
CN Cyclohexanecarboxamide, N-[cyano(2-methoxyphenyl)methyl]-2-[[4-[(4-fluorophenyl)methyl]-1-piperazinyl]carbonyl]-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



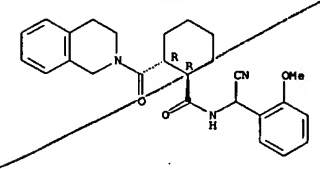
$R_1 = H$
$R_2 = \text{aryl}$.

RN 639792-02-2 CAPLUS

Karen Cheng

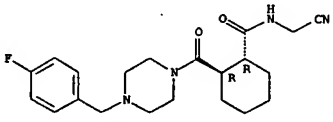
L11 ANSWER 32 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Cyclohexanecarboxamide, N-[cyano(2-methoxyphenyl)methyl]-2-[(3,4-dihydro-2(1H)-isoquinolinyl)carbonyl]-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 639792-03-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[4-[(4-fluorophenyl)methyl]-1-piperazinyl]carbonyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

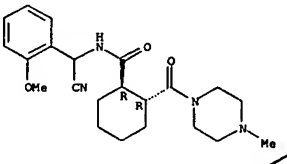
Relative stereochemistry.



$R_1 = R_2 = H$
$n = 2$
D = C sub. w/ keto.
E = heterocyclyl.
R_5 = C alkyl subst. w/ aryl

RN 639792-04-4 CAPLUS
CN Cyclohexanecarboxamide, N-[cyano(2-methoxyphenyl)methyl]-2-[(4-methyl-1-piperazinyl)carbonyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

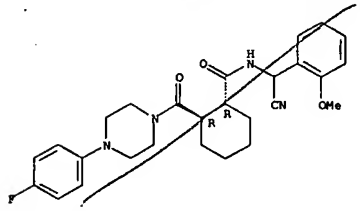
Relative stereochemistry.



RN 639792-05-5 CAPLUS
CN Cyclohexanecarboxamide, N-[cyano(2-methoxyphenyl)methyl]-2-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-, (1R,2R)- (9CI) (CA INDEX NAME)

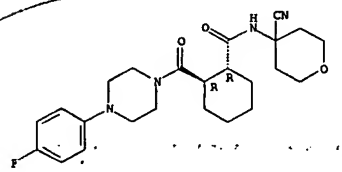
Absolute stereochemistry.

L11 ANSWER 32 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 639792-06-6 CAPLUS
CN Cyclohexanecarboxamide, N-(4-cyanotetrahydro-2H-pyran-4-yl)-2-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-, (1R,2R)- (9CI) (CA INDEX NAME)

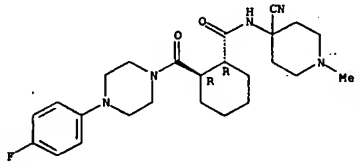
Absolute stereochemistry.



R1 & R2 = heterocycyl ring.
D = C alkyl w/ keto
E = heterocycyl
R5 = aryl.

RN 639792-07-7 CAPLUS
CN Cyclohexanecarboxamide, N-(4-cyano-1-methyl-4-piperidinyl)-2-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

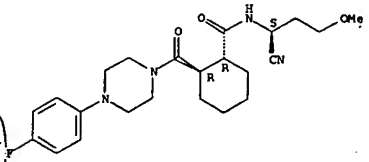


L11 ANSWER 32 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 32 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 639792-08-8 CAPLUS
CN Cyclohexanecarboxamide, N-[(1S)-1-cyano-3-methoxypropyl]-2-[[4-(4-fluorophenyl)-1-piperazinyl]carbonyl]-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

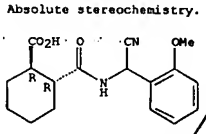


R1 = H
R2 = C1-6 alkyl subst. w/ OR6
R6 = alkyl.

IT 639792-09-9P 639792-10-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cyclohexane dicarboxamides for treating diseases associated with cysteine protease activity)

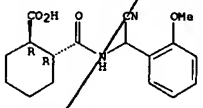
RN 639792-09-9 CAPLUS
CN Cyclohexanecarboxylic acid, 2-[[[cyano(2-methoxyphenyl)methyl]amino]carbonyl]-, (1R,2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 639792-10-2 CAPLUS
CN Cyclohexanecarboxylic acid, 2-[[[cyano(2-methoxyphenyl)methyl]amino]carbonyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

L11 ANSWER 33 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:737516 CAPLUS
DOCUMENT NUMBER: 139:257284
TITLE: Cathepsin cysteine protease inhibitors and their therapeutic use
INVENTOR(S): Bayly, Christopher I.; Black, Cameron; Leger, Serge; Li, Chun Sing; McKay, Dan; Mellon, Christophe; Gauthier, Jacques Yves; Lau, Cheuk; Therien, Michel; Truong, Vouy-Linh; Green, Michael J.; Hirschbein, Bernard L.; Janc, James W.; Palmer, James T.; Baskaran, Chitra
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.; Axys Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 282 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075836	A2	20030918	WO 2003-US6147	20030228
WO 2003075836	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2477657	A1	20030918	CA 2003-2477657	20030228
AU 2003219953	A1	20030922	AU 2003-219953	20030228
US 2003232863	A1	20031218	US 2003-377377	20030228
EP 1482924	A2	20041208	EP 2003-716238	20030228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008208	A	20050111	BR 2003-8208	20030228
CN 1638757	A	20050713	CN 2003-805181	20030228
JP 2005526753	T	20050908	JP 2003-574112	20030228
NZ 534583	A	20061130	NZ 2003-534583	20030228
US 2005240023	A1	20051027	US 2004-505796	20040825
NO 2004004207	A	20041124	NO 2004-4207	20041004
PRIORITY APPLN. INFO.:			US 2002-361818P P	20020305
			US 2002-408704P P	20020906
			WO 2003-US6147 W	20030228

OTHER SOURCE(S): MARPAT 139:257284

AB This invention relates to cysteine protease inhibitors R7(D)nCR6R7NR8CR3R4C(:O)NHCR1R2CN (R1-4 = H, (substituted)C1-6-alkyl or C2-6-alkenyl; R1 and R2 or R3 and R4 may be take together with the C atom to which they are attached to form a (substituted)C3-8-cycloalkyl or heterocyclic ring; R5 = H, (substituted)C1-6-alkyl; R6 = (substituted)aryl, heteroaryl, C1-6-haloalkyl, arylalky, heteroarylalkyl; D = (substituted)C1-3-alkyl, C2-3-alkenyl, C2-3-alkynyl, aryl, heteroaryl, C3-8-cycloalkyl, heterocyclyl; R7 = H, (substituted)C1-6-alkyl, C2-6-alkenyl, C2-6-alkynyl, C1-6-alkyloxy, etc.; R8 = H, C2-6-alkyl) including but not limited to, inhibitors of cathepsins K, L, S and B.

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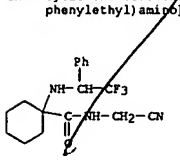
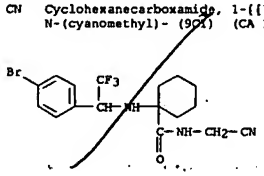
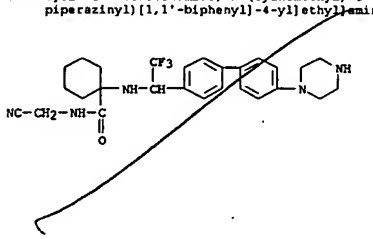
L11 ANSWER 33 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
These compds. are useful for treating diseases in which inhibition of bone resorption is indicated, such as osteoporosis.
IT 603140-31-4P 603140-32-5P 603140-33-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cathepsin cysteine protease inhibitors and their therapeutic use)
RN 603140-31-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[(2,2,2-trifluoro-1-phenylethyl)amino]- (9CI) (CA INDEX NAME)



RN 603140-32-5 CAPLUS
CN Cyclohexanecarboxamide, 1-[[1-(4-bromophenyl)-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



RN 603140-33-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[[2,2,2-trifluoro-1-[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]- (9CI) (CA INDEX NAME)

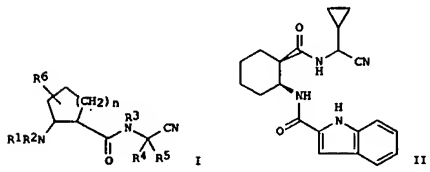


L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:454289 CAPLUS
DOCUMENT NUMBER: 139:36449
TITLE: Substituted 2-aminocycloalkanecarboxamides for use as cysteine protease inhibitors
INVENTOR(S): Gabriel, Thomas; Krauss, Nancy Elisabeth; Mirzadegan, Taraneh; Palmer, Wylie Solang; Smith, David Bernard
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003048123	A1	20030612	WO 2002-EP13221	20021125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2467435	A1	20030612	CA 2002-2467435	20021125
AU 2002352126	A1	20030617	AU 2002-352126	20021125
EP 1453801	A1	20040908	EP 2002-787799	20021125
EP 1453801	B1	20070321		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002014642	A	20041103	BR 2002-14642	20021125
HU 200402344	A2	20050228	HU 2004-2344	20021125
JP 2005517640	T	20050616	JP 2003-549315	20021125
CN 1639119	A	20050713	CN 2002-824060	20021125
AT 357432	T	20070415	AT 2002-787799	20021125
IN 2004CN01215	A	20060210	IN 2004-CN1215	20040602
NO 2004002719	A	20040628	NO 2004-2719	20040628
PRIORITY APPLN. INFO.:			US 2001-336750P	P 20011204
			WO 2002-EP13221	W 20021125

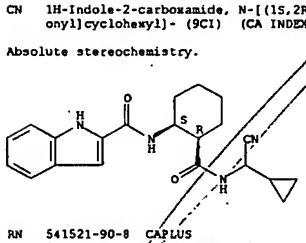
OTHER SOURCE(S): MARPAT 139:36449
GI

L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



AB Title compds. I [R1 = heteroaryl, (CR7R8)mCOR9, S(O)pR9; R2-R4, R6-R8 = H, alkyl; R5 = H, alkyl, heterocyclic, cycloalkyl, cycloalkylalkyl, alkoxycarbonylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl; R9 = heteroaryl, heteroarylalkyl, heteroarylalkoxy; m = 0, 1; n = 1-3; p = 1, 2] were prepared for use as cysteine protease inhibitors. The compds. are useful for the treatment of diseases which are associated with cysteine proteases such as osteoporosis, osteoarthritis, rheumatoid arthritis, tumor metastasis, glomerulonephritis, atherosclerosis, myocardial infarction, angina pectoris, instable angina pectoris, stroke, plaque rupture, transient ischemic attacks, amaurosis fugax, peripheral arterial occlusive disease, restenosis after angioplasty and stint placement, abdominal aortic aneurysm formation, inflammation, autoimmune disease, malaria, ocular fundus tissue cytopathy and respiratory disease. Thus, Et (1R,2S)-2-aminocyclohexanecarboxylate-HBr was treated with indole-2-carboxylic acid, followed by ester hydrolysis and amidation with (R,S)-amino(cyclopropyl)acetonitrile to give the amide II which had IC50 for inhibition of cathepsin K of 0.018 mM.
IT 541521-88-4P 541521-90-8P 541521-94-2P 541521-97-5P 541522-10-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted 2-aminocycloalkanecarboxamides for use as cysteine protease inhibitors)
RN 541521-88-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

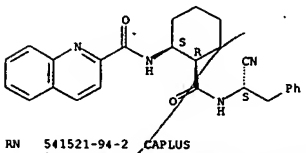
Absolute stereochemistry.



RN 541521-90-8 CAPLUS
CN 2-Quinolinecarboxamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-2-

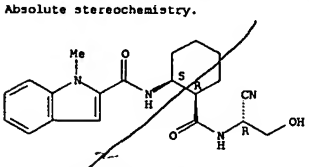
L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
phenylethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 541521-94-2 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[[(1R)-1-cyano-2-hydroxyethyl]amino]carbonyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

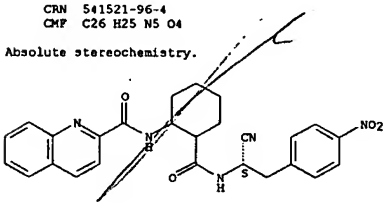


RN 541521-97-5 CAPLUS
CN 2-Quinolinecarboxamide, N-[2-[[[(1S)-1-cyano-2-(4-nitrophenyl)ethyl]amino]carbonyl]cyclohexyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 541521-96-4
CMF C26 H25 N5 O4

Absolute stereochemistry.



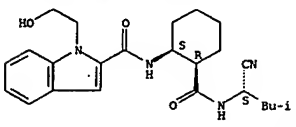
CM 2

CRN 76-05-1
CMF C2 H F3 O2

L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

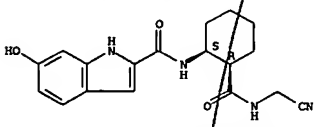
RN 541522-10-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-1-(2-hydroxyethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 541522-48-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted 2-aminocycloalkanecarboxamides for use as cysteine protease inhibitors)
RN 541522-48-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-6-hydroxy- (9CI) (CA INDEX NAME)

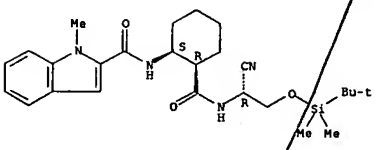
Absolute stereochemistry.



IT 541522-40-1P 541522-77-4P 541522-79-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted 2-aminocycloalkanecarboxamides for use as cysteine protease inhibitors)
RN 541522-40-1 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[[(1R)-1-cyano-2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]amino]carbonyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

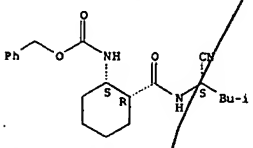
Absolute stereochemistry.

L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



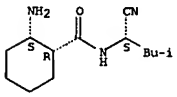
RN 541522-77-4 CAPLUS
CN Carbamic acid, [(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 541522-79-6 CAPLUS
CN Cyclohexanecarboxamide, 2-amino-N-[(1S)-1-cyano-3-methylbutyl]-, monohydrochloride, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IT 541521-92-0P 541521-99-7P 541522-01-4P
541522-04-7P 541522-06-9P 541522-08-1P
541522-91-2P 541522-93-4P 541522-95-6P
541522-98-9P 541523-01-7P 541523-03-9P
541523-04-0P 541523-06-2P 541523-07-3P
541523-10-8P 541523-12-0P 541523-13-1P
541523-15-3P 541523-18-6P 541523-19-7P

L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
541523-21-1P 541523-23-3P 541523-25-5P
541523-27-7P 541523-28-8P 541523-30-2P
541523-33-5P 541523-35-7P 541523-36-8P
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541523-44-8P 541523-46-0P 541523-48-2P
541523-50-6P 541523-52-8P 541523-54-0P
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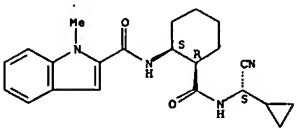
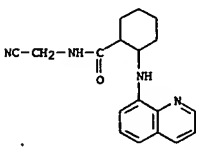
541523-62-0P 541523-64-2P 541523-66-4P
541523-68-6P 541523-71-1P 541524-25-8P
541524-27-0P 541524-29-2P 541524-31-6P
541524-33-8P 541524-35-0P 541524-37-2P
541524-39-4P 541524-41-8P 541524-44-1P
541524-46-3P 541524-48-5P 541524-50-9P
541524-52-1P 541524-55-4P 541524-57-6P
541524-59-8P 541524-62-3P 541524-64-5P
541524-67-8P 541524-70-3P 541524-72-5P
541524-74-7P 541524-76-9P 541524-78-1P
541524-81-6P 541524-83-8P 541524-86-1P
541524-88-3P 541524-90-7P 541524-92-9P
541524-94-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted 2-aminocycloalkanecarboxamides for use as cysteine protease inhibitors)
RN 541521-92-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[[(S)-cyanocyclopropylmethyl]amino]carbonyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



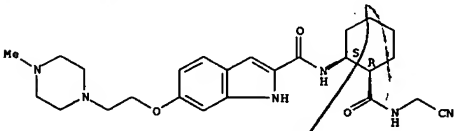
RN 541521-99-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-(8-quinolinylamino)- (9CI) (CA INDEX NAME)



RN 541522-01-4 CAPLUS

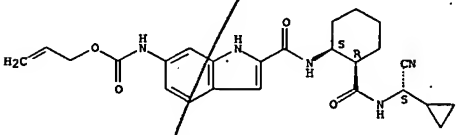
L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-6-[2-(4-methyl-1-piperazinyl)ethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



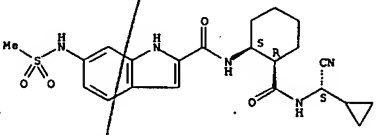
RN 541522-04-7 CAPLUS
CN Carbamic acid, [2-[[[(1S,2R)-2-[[[(S)-cyanocyclopropylmethyl]amino]carbonyl]cyclohexyl]amino]carbonyl]-1H-indol-6-yl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 541522-06-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[[(S)-cyanocyclopropylmethyl]amino]carbonyl]cyclohexyl]-6-[(methylsulfonyl)amino]- (9CI) (CA INDEX NAME)

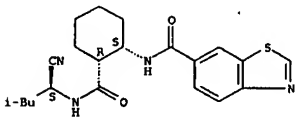
Absolute stereochemistry.



RN 541522-08-1 CAPLUS
CN 6-Benzothiazolecarboxamide, N-[(1S,2R)-2-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

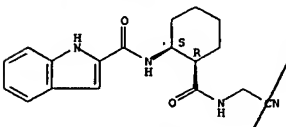
Absolute stereochemistry.

L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



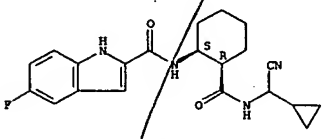
RN 541522-91-2 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanomethyl)amino]carbonyl]cycloh exyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 541522-93-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carb onyl]cyclohexyl]-5-fluoro- (9CI) (CA INDEX NAME)

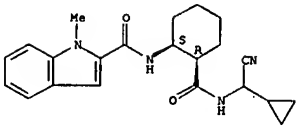
Absolute stereochemistry.



RN 541522-95-6 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carb onyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

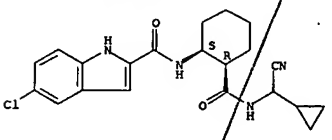
Absolute stereochemistry.

L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



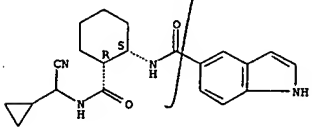
RN 541522-98-9 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 541523-01-7 CAPLUS
CN 1H-Indole-5-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carb onyl]cyclohexyl]- (9CI) (CA INDEX NAME)

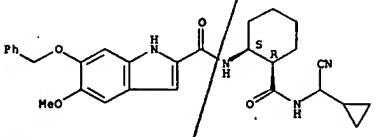
Absolute stereochemistry.



RN 541523-03-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carb onyl]cyclohexyl]-5-methoxy-6-(phenylmethoxy)- (9CI) (CA INDEX NAME)

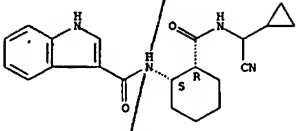
Absolute stereochemistry.

L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



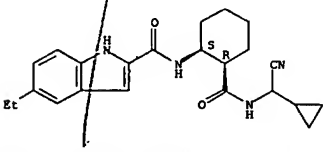
RN 541523-04-0 CAPLUS
CN 1H-Indole-3-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carb onyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 541523-06-2 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carb onyl]cyclohexyl]-5-ethyl- (9CI) (CA INDEX NAME)

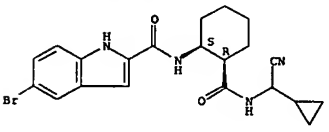
Absolute stereochemistry.



RN 541523-07-3 CAPLUS
CN 1H-Indole-2-carboxamide, 5-bromo-N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

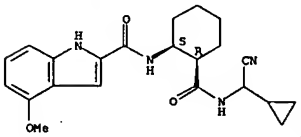
Absolute stereochemistry.

L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



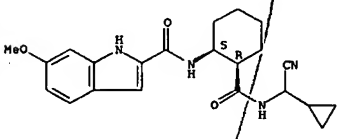
RN 541523-10-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carb onyl]cyclohexyl]-4-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 541523-12-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carb onyl]cyclohexyl]-6-methoxy- (9CI) (CA INDEX NAME)

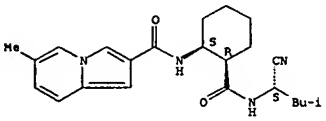
Absolute stereochemistry.



RN 541523-13-1 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-2-[[(cyanocyclopropylmethyl)amino]carb onyl]cyclohexyl]-5-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L11 ANSWER 34 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:396667 CAPLUS
DOCUMENT NUMBER: 138:401413
TITLE: Preparation of aryl-containing N-cyanoalkyl carboxamides as protease inhibitors
INVENTOR(S): Black, Cameron; Crane, Sheldon N.; Davis, Dana; Setti, Eduardo L.
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.; Axys Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003041649	A2	20030522	WO 2002-US36352	20021113
WO 2003041649	A3	20030731		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2466115	A1	20030522	CA 2002-2466115	20021113
AU 2002352663	A1	20030526	AU 2002-352663	20021113
EP 1446115	A2	20040818	EP 2002-789611	20021113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005521639	T	20050721	JP 2003-543536	20021113
US 2005014941	A1	20050120	US 2004-495387	20040511
PRIORITY APPLN. INFO.:			US 2001-351316P	P 20011113
			WO 2002-US36352	W 20021113

OTHER SOURCE(S): MARPAT 138:401413

AB The present invention is directed to aryl-containing N-cyanoalkyl carboxamides, Ar-X1-CR4R5CHR6CHR6aC(O)NR3CR1R2CN (I; variables defined below; e.g. trans-N-cyanomethyl-2-[(4-fluorophenylsulfanyl)methyl]cyclohex anecarboxamide), that are inhibitors of cysteine proteases such as cathepsins K, S, B and L, in particular cathepsin K (only a qual. statement of activity is indicated). Pharmaceutical composition comprising these compds., method of treating diseases (e.g. osteoporosis) mediated by unregulated cysteine protease activity, in particular cathepsin K, using these compds. and methods of preparing these compds. are also disclosed. Thirty-eight example prepns. of I are included. For example, trans-N-cyanomethyl-2-[(4-fluorophenylsulfanyl)methyl]cyclohexanecarboxami de was prepared in 3 steps starting from trans-1,2-cyclohexanedicarboxylic anhydride, aminoacetonitrile hydrochloride, Et3N, and iBu chloroformate in THF involving intermediates trans-N-cyanomethyl-2-hydroxymethylcyclohexanecarboxamide and trans-2-bromomethyl-N-cyanomethylcyclohexanecarboxamide (yields not given). Three

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pharmaceutical formulations contg. I are described. For I: X1 is -O-, -NR-, -S-, -S(O)- or -S(O)2- (R is H, (C1-6)alkyl, halo-substituted(C1-6)alkyl, or aryl(C1-6)alkyl); R1 is H or (C1-6)alkyl; R2 is H, (C1-6)alkyl, halo-substituted (C1-3)alkyl, -X2NR7R7, -X2NR7C(O)R7, -X2C(O)NR7R7, -X2NR7C(O)OR7, - X2OC(O)NR7R7, -X2NR7C(O)NR7R7, -X2NR7C(NR7)NR7R7, -X2OR7, -X2C(O)R7, -X2C(O)OR7, -X2OC(O)R7, -X2S(O)2NR7R7, -X2P(O)(OR7)OR7, -X2OP(O)(OR7)OR7, -X2SR7, -X2S(O)R8, -X2S(O)2R8, -X2NR7S(O)2R8, -X2NR9R10, -X2NR9C(O)R10, -X2C(O)NR9R10, -X2S(O)2NR9R10, -X2NR9S(O)2R10, -X2OC(O)NR9R10, -X2NR9C(O)NR9R10, -X2NR9C(NR9)NR9R10, -R10, -X2OR10, -X2C(O)R10, -X2C(O)OR10, -X2OC(O)R10, -X2SR10, -X2S(O)R10, and -X2S(O)2R10; or R1 and R2 together with the C atoms to which they are attached form (C3-8)monocyclic cycloalkylene or monocyclic heterocycloalkylene. R3 is H or (C1-6)alkyl; R6 and R6a together with the C atoms to which they are attached form: (C3-7) monocyclic cycloalkylene, (C7-8) bridged polycyclic cycloalkylene, (C3-7) monocyclic cycloalkenylene, (C7-8) bridged polycyclic cycloalkenylene, (C7-8) spirocycloalkylene, monocyclic heterocycloalkylene having 3-7 ring atoms, bridged polycyclic heterocycloalkylene having 7 or 8 ring atoms, monocyclic heterocycloalkenylene having 3-7 ring atoms, bridged polycyclic heterocycloalkenylene having 7 or 8 ring atoms, phenylene, or heteroarylene having 5 or 6 ring atoms. R4 and R5 are each independently H, fluoro or (C1-6)alkyl or R4 and R5 together with the C atoms to which they are attached form (C3-6) monocyclic cycloalkylene or monocyclic heterocycloalkylene having 3 to 6 ring atoms; Ar = (C0-3)alkylene-Ar1 (Ar1 is (C6-12)aryl, heteroaryl, heterocycloalkyl, or heterocycloalkenyl), (C0-3)alkylene-Ar1-X4-Ar2, (C0-3)alkylene-Ar1-X4-Ar2-X5-Ar3, (C0-3)alkylene-Ar1-X4-Ar2-X5-Ar3-X6-Ar4 (X4, X5 and X6 = a bond, (C1-6)alkylene, etc.); Ar2, Ar3 and Ar4 = (C3-8)cycloalkyl, (C3-8)cycloalkenyl, heterocycloalkyl, heterocycloalkenyl, (C6-14)aryl and heteroaryl; addnl. details are given in the claims.

IT 530104-11-1P, trans-N-Cyanomethyl-2-[(4-fluorophenylsulfanyl)methyl]cyclohexanecarboxamide 530104-17-7P, trans-N-Cyanomethyl-2-[(4-bromophenylsulfanyl)methyl]cyclohexanecarboxamid e 530104-38-2P, trans-N-Cyanomethyl-2-[[[4-[4-(4-tert-butoxycarbonylpiperazin-1-yl)phenyl]phenyl]sulfanyl]methyl]cyclohexanecarb oxamide 530104-43-9P, trans-N-Cyanomethyl-2-[(4-fluorobenzenesulfonyl)methyl]cyclohexanecarboxamide 530104-63-3P , trans-N-Cyanomethyl-2-[[4-(carboxymethylsulfanyl)benzenesulfonyl]methyl] cyclohexanecarboxamide 530104-82-6P, trans-N-Cyanomethyl-2-[[4-(methylsulfanyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530105-48-7P, (1R/S,2R/S,3R/S,4S/R)-N-(Cyanomethyl)-3-[[(4-fluorophenyl)sulfanyl]methyl]bicyclo[2.2.1]hept-5-ene-2-carboxamide 530105-53-4P, (1S/R,2R/S,3R/S,4R/S)-N-(Cyanomethyl)-3-[[(4-fluorophenyl)sulfanyl]methyl]bicyclo[2.2.1]heptane-2-carboxamide 530105-55-6P, (1S/R,2R/S,3R/S,4R/S)-N-(Cyanomethyl)-3-[[4-fluorobenzenesulfonyl)methyl]bicyclo[2.2.1]heptane-2-carboxamide 530105-58-9P, (5R/S,6R/S)-N-(Cyanomethyl)-6-[[(4-fluorophenyl)sulfanyl]methyl]spiro[2.4]heptane-5-carboxamide 530105-73-8P, (1R/S,6R/S)-N-(Cyanomethyl)-6-[[(4-fluorophenyl)sulfanyl]methyl]cyclohex-3-ene-1-carboxamide 530105-81-8P, (1R/S,6R/S)-N-(Cyanomethyl)-6-[[(4-fluorobenzene)sulfonyl]methyl]cyclohex-3-ene-1-carboxamide 530106-10-6P, (1R/S,2R/S,3R/S,6S/R)-N-(Cyanomethyl)-3-[[(4-fluorophenyl)sulfanyl]methyl]bicyclo[4.1.0]heptane-2-carboxamide 530106-16-2P, (1R/S,2R/S,3R/S,6S/R)-N-(Cyanomethyl)-3-[(4-fluorobenzenesulfonyl)methyl]bicyclo[4.1.0]heptane-2-carboxamide 530106-37-7P, trans-N-Cyanomethyl-2-[(4-[[2-(tert-butoxycarbonylamino)ethyl]sulfanyl]benzenesulfonyl]methyl)cyclohexanecarbo xamide 530106-43-5P 530106-77-5P, trans-N-Cyanomethyl-

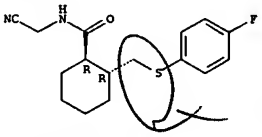
Karen Cheng

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

2-[(4-hydroxymethylbenzenesulfonyl)methyl]cyclohexanecarboxamide 530106-83-3P, trans-N-Cyanomethyl-2-[(4-[(benzylsulfanyl)methyl]benzenesulfonyl)methyl]cyclohexanecarboxamide RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (drug candidate; prepn. of aryl-contg. N-cyanoalkyl carboxamides as protease inhibitors)

RN 530104-11-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-fluorophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

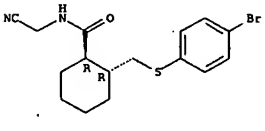
Relative stereochemistry.



no S for Dan E

RN 530104-17-7 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(4-bromophenyl)thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

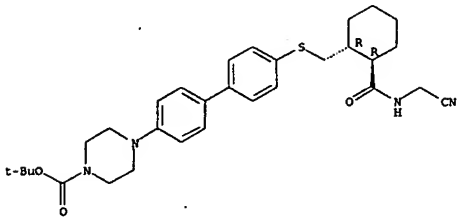
Relative stereochemistry.



RN 530104-38-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4'-[[[(1R,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]methyl]thio][1,1'-biphenyl]-4-yl]-, 1,1-dimethylethyl ester, rel- (9CI) (CA INDEX NAME)

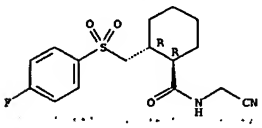
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



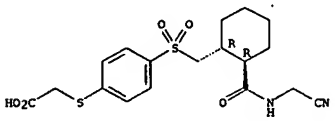
RN 530104-43-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4- , fluorophenyl)sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-63-3 CAPLUS
CN Acetic acid, [[4-[[[(1R,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]methyl]sulfonyl]phenyl]thio]-, rel- (9CI) (CA INDEX NAME)

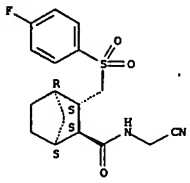
Relative stereochemistry.



RN 530104-82-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(methylthio)phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

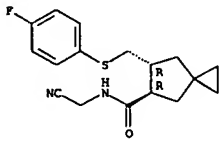
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



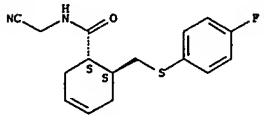
RN 530105-58-9 CAPLUS
CN Spiro[2.4]heptane-5-carboxamide, N-(cyanomethyl)-6-[[(4-fluorophenyl)thio]methyl]-, (5R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530105-73-8 CAPLUS
CN 3-Cyclohexene-1-carboxamide, N-(cyanomethyl)-6-[[(4-fluorophenyl)thio]methyl]-, (1R,6R)-rel- (9CI) (CA INDEX NAME)

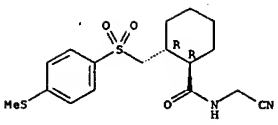
Relative stereochemistry.



RN 530105-81-8 CAPLUS
CN 3-Cyclohexene-1-carboxamide, N-(cyanomethyl)-6-[[(4-fluorophenyl)sulfonyl]methyl]-, (1R,6R)-rel- (9CI) (CA INDEX NAME)

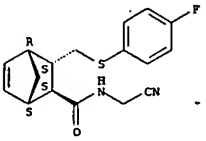
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



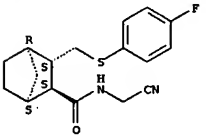
RN 530105-48-7 CAPLUS
CN Bicyclo[2.2.1]hept-5-ene-2-carboxamide, N-(cyanomethyl)-3-[[(4-fluorophenyl)thio]methyl]-, (1R,2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530105-53-4 CAPLUS
CN Bicyclo[2.2.1]heptane-2-carboxamide, N-(cyanomethyl)-3-[[(4-fluorophenyl)thio]methyl]-, (1R,2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

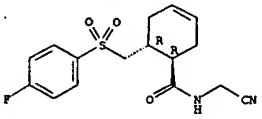
Relative stereochemistry.



RN 530105-55-6 CAPLUS
CN Bicyclo[2.2.1]heptane-2-carboxamide, N-(cyanomethyl)-3-[[(4-fluorophenyl)sulfonyl]methyl]-, (1R,2R,3R,4S)-rel- (9CI) (CA INDEX NAME)

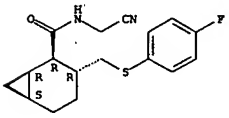
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



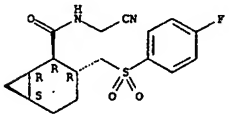
RN 530106-10-6 CAPLUS
CN Bicyclo[4.1.0]heptane-2-carboxamide, N-(cyanomethyl)-3-[[(4-fluorophenyl)thio]methyl]-, (1R,2R,3R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530106-16-2 CAPLUS
CN Bicyclo[4.1.0]heptane-2-carboxamide, N-(cyanomethyl)-3-[[(4-fluorophenyl)sulfonyl]methyl]-, (1R,2R,3R,6S)-rel- (9CI) (CA INDEX NAME)

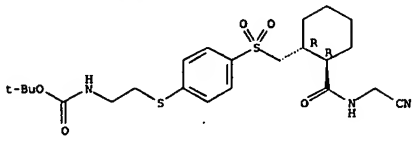
Relative stereochemistry.



RN 530106-37-7 CAPLUS
CN Carbamic acid, [2-[[4-[[[(1R,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]methyl]sulfonyl]phenyl]thio]ethyl]-, 1,1-dimethylethyl ester, rel- (9CI) (CA INDEX NAME)

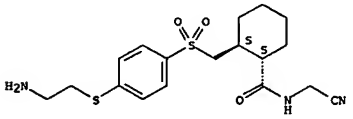
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



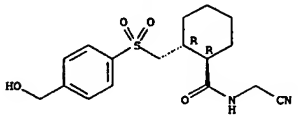
RN 530106-43-5 CAPLUS
CN Cyclohexanecarboxamide, 2-[[[4-[(2-aminoethyl)thio]phenyl]sulfonyl]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530106-77-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(hydroxymethyl)phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

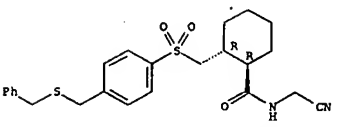
Relative stereochemistry.



RN 530106-83-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[(phenylmethyl)thio]methyl]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



IT 530104-19-9P, trans-N-Cyanomethyl-2-[(phenylsulfanyl)methyl]cyclohexanecarboxamide 530104-21-3P, trans-N-Cyanomethyl-2-[(4-chlorophenylsulfanyl)methyl]cyclohexanecarboxamide 530104-23-5P, trans-N-Cyanomethyl-2-[(3,4-dichlorophenylsulfanyl)methyl]cyclohexanecarboxamide 530104-25-7P, trans-N-Cyanomethyl-2-[[(4-methylphenyl)sulfanyl]methyl]cyclohexanecarboxamide 530104-27-9P, trans-N-Cyanomethyl-2-[(4-methoxyphenylsulfanyl)methyl]cyclohexanecarboxamide 530104-28-0P, trans-N-Cyanomethyl-2-[[4-(morpholino)phenylsulfanyl]methyl]cyclohexanecarboxamide 530104-30-4P, trans-N-Cyanomethyl-2-[[(4-methylcarbonylaminophenyl)sulfanyl]methyl]cyclohexanecarboxamide 530104-32-6P, trans-N-Cyanomethyl-2-[(4-nitrophenylsulfanyl)methyl]cyclohexanecarboxamide 530104-34-8P, trans-N-Cyanomethyl-2-[[(4-tert-butylphenyl)sulfanyl]methyl]cyclohexanecarboxamide 530104-36-0P, trans-N-Cyanomethyl-2-[[(4-trifluoromethylphenyl)sulfanyl]methyl]cyclohexanecarboxamide 530104-42-8P, trans-N-Cyanomethyl-2-[[[4-(4-(piperazin-1-yl)phenyl)phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530104-45-1P, trans-N-Cyanomethyl-2-[(4-bromobenzenesulfonyl)methyl]cyclohexanecarboxamide 530104-47-3P, trans-N-Cyanomethyl-2-[[4-(morpholino)benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-49-5P, trans-N-Cyanomethyl-2-[(benzenesulfonyl)methyl]cyclohexanecarboxamide 530104-51-9P, trans-N-Cyanomethyl-2-[(4-chlorobenzenesulfonyl)methyl]cyclohexanecarboxamide 530104-53-1P, trans-N-Cyanomethyl-2-[(3,4-dichlorobenzenesulfonyl)methyl]cyclohexanecarboxamide 530104-55-3P, trans-N-Cyanomethyl-2-[(4-methylbenzenesulfonyl)methyl]cyclohexanecarboxamide 530104-57-5P, trans-N-Cyanomethyl-2-[(4-methoxybenzenesulfonyl)methyl]cyclohexanecarboxamide 530104-59-7P, trans-N-Cyanomethyl-2-[(4-bromophenylsulfinyl)methyl]cyclohexanecarboxamide 530104-61-1P, trans-N-Cyanomethyl-2-[[4-[((ethoxycarbonyl)methyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-67-7P, trans-N-Cyanomethyl-2-[[4-[[[(pyridin-4-ylmethyl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-69-9P, trans-N-Cyanomethyl-2-[[4-[[[[(2-(thien-2-yl)ethyl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-71-3P, trans-N-Cyanomethyl-2-[[4-[[[(2-chlorobenzylamino)carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-73-5P, trans-N-Cyanomethyl-2-[[4-[[[(4-methoxybenzylamino)carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-74-6P, trans-N-Cyanomethyl-2-[[4-[[[(4-chlorobenzylamino)carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-76-8P, trans-N-Cyanomethyl-2-[[4-[[[[(3-dimethylaminobenzyl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]

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methyl]cyclohexanecarboxamide 530104-78-0P, trans-N-Cyanomethyl-2-[[4-[[(4-(pyridin-4-yl)piperazin-1-ylcarbonyl)methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-80-4P, trans-N-Cyanomethyl-2-[[4-[[[[(1-benzylpiperidin-4-yl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-84-8P, trans-N-Cyanomethyl-2-[[4-[(3-hydroxypropyl)sulfanyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-86-0P, trans-N-Cyanomethyl-2-[[(4-methylsulfanylphenyl)sulfanyl]methyl]cyclohexanecarboxamide 530104-88-2P, trans-N-Cyanomethyl-2-[(4-hydroxyphenylsulfanyl)methyl]cyclohexanecarboxamide 530104-91-7P, trans-N-Cyanomethyl-2-[[[4-[(4-sulfanylphenyl)sulfanyl]phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530104-96-2P, trans-N-Cyanomethyl-2-[[4-[(furan-2-ylmethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530104-99-5P, trans-N-Cyanomethyl-2-[[4-[[[[(2-morpholinoethyl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530105-00-1P, trans-N-Cyanomethyl-2-[[4-[[[[(2-morpholinoethyl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide trifluoroacetate 530105-06-7P, trans-N-Cyanomethyl-2-[[4-[[[(pyridin-3-ylamino)carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide trifluoroacetate 530105-10-3P, trans-N-Cyanomethyl-2-[[4-[[(4-isopropylpiperazin-1-ylcarbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530105-11-4P, trans-N-Cyanomethyl-2-[[4-[[(4-isopropylpiperazin-1-ylcarbonyl)methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide trifluoroacetate 530105-13-6P, trans-N-(Cyanomethyl)-2-[[[4-(methylsulfanyl)phenyl]sulfanyl]methyl]cyclopentanecarboxamide 530105-24-9P, (1S/R,3R/S,4R/S,6R/S)-N-(Cyanomethyl)-4-[[[4-(methylsulfanyl)phenyl]sulfanyl]methyl]bicyclo[4.1.0]heptane-3-carboxamide 530105-37-4P, (1R/S,2R/S,3R/S,4S/R)-N-(Cyanomethyl)-3-[(4-fluorobenzenesulfonyl)methyl]bicyclo[2.2.1]hept-5-ene-2-carboxamide 530105-49-0P, (1S/R,2R/S,3R/S,4R/S)-N-(Cyanomethyl)-3-[[4-(methylsulfanyl)benzenesulfonyl]methyl]bicyclo[2.2.1]heptane-2-carboxamide 530105-71-6P, (5R/S,6R/S)-N-(Cyanomethyl)-6-[[(4-fluorobenzene)sulfonyl]methyl]spiro[2.4]heptane-5-carboxamide 530105-79-4P, (1R/S,6R/S)-N-(Cyanomethyl)-6-[[[4-(methylsulfanyl)benzene]sulfonyl]methyl]cyclohex-3-ene-1-carboxamide 530105-83-0P, (1R,2R)-N-(Cyanomethyl)-2-[[[4-(methylsulfanyl)benzene]sulfonyl]methyl]cyclohexanecarboxamide 530105-94-3P, (1R/S,2S/R,3S/R,6S/R)-N-(Cyanomethyl)-3-[[(4-methylsulfanylbenzene)sulfonyl]methyl]bicyclo[4.1.0]heptane-2-carboxamide 530106-18-4P, (1R/S,2R/S)-N-(Cyanomethyl)-5-methyl-2-[[[4-(methylsulfanyl)benzene]sulfonyl]methyl]cyclohexanecarboxamide 530106-35-5P, trans-N-Cyanomethyl-2-[[4-[(2-phenylethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530106-41-3P, trans-N-Cyanomethyl-2-[[4-[(2-(pyridin-2-yl)ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530106-44-6P, trans-N-Cyanomethyl-2-[[4-[(2-aminoethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide mesylate 530106-47-9P, trans-N-Cyanomethyl-2-[[4-[(2-[(2-chloropyridin-3-yl)amino]ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide mesylate 530106-51-5P, trans-N-Cyanomethyl-2-[[4-[[2-[(pyridin-4-yl)amino]ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide mesylate 530106-54-8P, trans-N-Cyanomethyl-2-[[3-fluoro-4-[[2-[(dimethylaminosulfonyl)amino]ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide mesylate 530106-61-7P, trans-N-Cyanomethyl-2-[[3-fluoro-4-[(2-aminoethyl)sulfanyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530106-64-0P, trans-N-Cyanomethyl-2-[(3-fluoro-4-[(2-(pyridin-2-yl)ethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide

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530106-65-1P, trans-N-Cyanomethyl-2-[[3-fluoro-4-[[2-(pyridin-2-yl)ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide mesylate 530106-67-3P, trans-2-[[4-[[2-(Pyridin-2-yl)ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxylic acid 1-cyanocyclopropylamide 530106-87-7P, trans-N-Cyanomethyl-2-[[4-[(benzylsulfonyl)methyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530106-89-9P, trans-N-Cyanomethyl-2-[(4-methylcarbonylaminobenzenesulfonyl)methyl]cyclohexanecarboxamide 530106-91-3P, trans-N-Cyanomethyl-2-[(4-nitrobenzenesulfonyl)methyl]cyclohexanecarboxamide 530106-93-5P, trans-N-Cyanomethyl-2-[(4-tert-butylbenzenesulfonyl)methyl]cyclohexanecarboxamide 530106-95-7P, trans-N-Cyanomethyl-2-[[4-(methylsulfonyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530106-97-9P, trans-N-Cyanomethyl-2-[[(1-methylimidazol-2-yl)sulfanyl]methyl]cyclohexanecarboxamide 530106-99-1P, trans-N-Cyanomethyl-2-[(4-aminobenzenesulfonyl)methyl]cyclohexanecarboxamide 530107-01-8P, trans-N-Cyanomethyl-2-[(benzothiazol-2-ylsulfanyl)methyl]cyclohexanecarboxamide 530107-03-0P, trans-N-Cyanomethyl-2-[(benzoxazol-2-ylsulfanyl)methyl]cyclohexanecarboxamide 530107-05-2P, trans-N-Cyanomethyl-2-[(4,5-dihydrothiazol-2-ylsulfanyl)methyl]cyclohexanecarboxamide 530107-07-4P, trans-N-Cyanomethyl-2-[(4-trifluoromethylbenzenesulfonyl)methyl]cyclohexanecarboxamide 530107-09-6P, trans-N-Cyanomethyl-2-[(pyrimidin-2-ylsulfanyl)methyl]cyclohexanecarboxamide 530107-11-0P, trans-N-Cyanomethyl-2-[(4-hydroxybenzenesulfonyl)methyl]cyclohexanecarboxamide 530107-13-2P, trans-N-Cyanomethyl-2-[[(1-methylimidazol-2-yl)sulfonyl]methyl]cyclohexanecarboxamide 530107-15-4P, trans-N-Cyanomethyl-2-[[4-[2-(4-isopropylpiperazin-1-yl)thiazol-4-yl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-17-6P, trans-N-Cyanomethyl-2-[(pyridin-4-ylsulfanyl)methyl]cyclohexanecarboxamide 530107-18-7P, trans-N-Cyanomethyl-2-[(6-chlorobenzoxazol-2-ylsulfanyl)methyl]cyclohexanecarboxamide 530107-20-1P, trans-N-Cyanomethyl-2-[(5-methoxybenzothiazol-2-ylsulfanyl)methyl]cyclohexanecarboxamide 530107-22-3P, trans-N-Cyanomethyl-2-[(4-methoxybenzylsulfanyl)methyl]cyclohexanecarboxamide 530107-24-5P, trans-N-Cyanomethyl-2-[[(2-pyridin-4-yl-1,3,4-oxadiazol-5-yl)sulfanyl]methyl]cyclohexanecarboxamide 530107-26-7P, trans-N-Cyanomethyl-2-[(pyridin-4-ylsulfonyl)methyl]cyclohexanecarboxamide 530107-28-9P, trans-N-Cyanomethyl-2-[(2,4-dichlorobenzylsulfanyl)methyl]cyclohexanecarboxamide 530107-30-3P, trans-N-Cyanomethyl-2-[(2,4-dichlorophenylsulfanyl)methyl]cyclohexanecarboxamide 530107-32-5P, trans-N-Cyanomethyl-2-[[4-[[(1-methylpyrrolidin-2-yl)methyl]oxy]phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530107-34-7P, trans-N-Cyanomethyl-2-[[(4-dimethylaminophenyl)sulfanyl]methyl]cyclohexanecarboxamide 530107-36-9P, trans-N-Cyanomethyl-2-[(4-dimethylaminobenzenesulfonyl)methyl]cyclohexanecarboxamide 530107-38-1P, trans-N-Cyanomethyl-2-[(4-trifluoromethoxyphenylsulfanyl)methyl]cyclohexanecarboxamide 530107-40-5P, trans-N-Cyanomethyl-2-[(3,4-dimethoxyphenylsulfanyl)methyl]cyclohexanecarboxamide 530107-41-6P, trans-N-Cyanomethyl-2-[[[4-[(1-methylpiperidin-4-yl)oxy]phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530107-43-8P, trans-N-Cyanomethyl-2-[[[4-[(3-dimethylaminopropyl)oxy]phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530107-45-0P 530107-47-2P, trans-N-Cyanomethyl-2-[[4-(1-methylpiperazin-4-yl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-49-4P, trans-N-Cyanomethyl-2-[[4-(4-morpholinopiperidin-1-yl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-51-8P,

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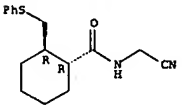
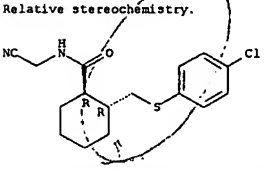
trans-N-Cyanomethyl-2-[(4-methoxyphenylsulfanyl)methyl]cyclopentanecarboxamide 530107-53-0P, trans-N-Cyanomethyl-2-[[4-(4-tert-butoxypiperidin-4-yloxy)phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530107-55-2P, trans-N-Cyanomethyl-2-[[4-(4-tert-butoxypiperidin-4-yloxy)benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-58-5P, trans-N-Cyanomethyl-2-[(cyclohexylsulfanyl)methyl]cyclohexanecarboxamide 530107-61-0P, trans-N-Cyanomethyl-2-[[(3-carboxymethylphenyl)sulfanyl]methyl]cyclohexanecarboxamide 530107-63-2P, trans-N-Cyanomethyl-2-[(4-(thien-3-yl)benzenesulfonyl)methyl]cyclohexanecarboxamide 530107-65-4P, trans-N-Cyanomethyl-2-[[(3-trifluoroacetylaminophenyl)sulfanyl]methyl]cyclohexanecarboxamide 530107-67-6P, trans-N-Cyanomethyl-2-[[(3-(methylsulfonylamino)phenyl)sulfanyl]methyl]cyclohexanecarboxamide 530107-69-8P, (1S/R,3R/S,4S/R,6R/S)-4-[[(4-Methylsulfanylphenyl)sulfanyl]methyl]bicyclo[4.1.0]heptane-3-carboxylic acid cyanomethylamide 530107-71-2P, trans-N-Cyanomethyl-2-[[4-(4-((pyridin-4-yl)oxy)phenyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-73-4P, trans-N-Cyanomethyl-2-[[4-(3-aminophenyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-75-6P, trans-N-Cyanomethyl-2-[[4-(pyridin-4-ylsulfanyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-77-8P 530107-80-3P, trans-N-Cyanomethyl-2-[[4-[(2-chlorophenylmethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-82-5P, trans-N-Cyanomethyl-2-[[4-[(2-(2,2,2-trifluoroethylamino)ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-84-7P, trans-N-Cyanomethyl-2-[[4-[[[(pyridin-3-ylmethyl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-86-9P, trans-N-Cyanomethyl-2-[[4-[[2-(2-chloropyridin-3-ylcarbonyl)amino]ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-88-1P, trans-N-Cyanomethyl-2-[[4-[[2-[[(pyridin-4-yl)carbonyl]amino]ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-90-5P, trans-N-Cyanomethyl-2-[[4-[(2-acetylaminoethyl)oxy]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-92-7P, trans-N-Cyanomethyl-2-[[4-[[[[[(4-dimethylaminophenyl)methyl]amino]carbonyl]methyl]sulfanyl}benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-93-8P, trans-N-Cyanomethyl-2-[[4-[[[[(2-(pyridin-4-yl)ethyl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-95-0P, trans-N-Cyanomethyl-2-[[3-fluoro-4-[(2-(ethylsulfonylamino)ethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-97-2P, trans-N-Cyanomethyl-2-[[4-[[[[(furan-2-ylmethyl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530107-99-4P, trans-N-Cyanomethyl-2-[[3-fluoro-4-[(2-dimethylsulfonylaminoethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-01-1P, trans-N-Cyanomethyl-2-[[4-[(2-(methylsulfonyloxy)ethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-03-3P, trans-N-Cyanomethyl-2-[[4-(methoxycarbonylmethyloxy)benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-05-5P 530108-07-7P, trans-N-Cyanomethyl-2-[[4-[[(1-tert-butylpiperazin-4-ylcarbonyl)methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-09-9P, trans-N-Cyanomethyl-2-[[4-[[[1-(pyridin-2-yl)piperazin-4-yl]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-11-3P, trans-N-Cyanomethyl-2-[[4-[[(1-tert-butylpiperazin-4-ylcarbonyl)methyl]oxy]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-13-5P, trans-N-Cyanomethyl-2-[[4-[[[1-(pyrimidin-2-yl)piperazin-4-yl]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-15-7P, trans-N-Cyanomethyl-2-[[4-[[[[(2-(thien-2-yl)ethyl)amino]carbonyl]methyl]sulfonyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-16-8P, trans-N-Cyanomethyl-2-[[4-[[[1-(4-bromophenyl)piperazin-4-ylcarbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-18-0P, trans-N-Cyanomethyl-2-[[4-[[[[(2-(pyridin-4-yl)ethyl)amino]carbonyl]methyl]oxy]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-20-4P, 2-[[4-Fluorophenylsulfanyl)methyl]cyclohexanecarboxylic acid (1-cyanocyclopropyl)amide 530108-22-6P, trans-N-Cyanomethyl-2-[[4-[[[[[(3-methyl-1,2,5-oxadiazol-4-yl)methyl]amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-24-8P, trans-N-Cyanomethyl-2-[[4-[(2-((morpholinocarbonyl)amino)ethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-25-9P, trans-N-Cyanomethyl-2-[[4-[[2-(pyridin-3-yloxy)ethyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-27-1P, trans-N-Cyanomethyl-2-[[4-[(2-((morpholinocarbonyl)amino)ethyl)oxy]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-29-3P, trans-N-Cyanomethyl-2-[[4-[[[(furan-2-ylmethyl)amino]carbonyl]methyl]benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-31-7P, trans-N-Cyanomethyl-2-[[4-(2-((((furan-2-yl)methyl)amino)carbonyl)ethyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-33-9P, trans-N-Cyanomethyl-2-[[[4-(2-((((furan-2-yl)methyl)amino)carbonyl)ethyl)phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530108-35-1P, trans-N-Cyanomethyl-2-[[4-((2-bromoethyl)sulfanyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-41-9P 530108-45-3P, cis-N-Cyanomethyl-2-[[4-(methylsulfanyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-47-5P, trans-N-Cyanomethyl-2-[1-[4-(methylsulfanyl)benzenesulfonyl]ethyl]cyclohexanecarboxamide 530108-49-7P, trans-N-Cyanomethyl-2-[[[4-[3-[[(2-morpholinoethyl)amino]carbonyl]propyl]phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530108-53-3P, (1R/S,2R/S,5R/S)-Trans-N-cyanomethyl-2-[[4-(methylsulfanyl)benzenesulfonyl]methyl]-5-methylcyclohexanecarboxamide 530108-56-6P 530108-60-2P, trans-N-Cyanomethyl-2-[[3-((3-hydroxypropyl)sulfanyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530108-62-4P, trans-2-[[(4-Chlorophenyl)sulfanyl]methyl]-N-(cyanomethyl)cyclopentanecarboxamide 530108-63-5P, trans-N-(Cyanomethyl)-2-[[(4-fluorophenyl)sulfanyl]methyl]cyclopentanecarboxamide 530108-65-7P, trans-2-[[(3-Bromophenyl)sulfanyl]methyl]-N-(cyanomethyl)cyclohexanecarboxamide 530108-67-9P, trans-N-(Cyanomethyl)-2-[[(3-fluorophenyl)sulfanyl]methyl]cyclohexanecarboxamide 530108-69-1P, trans-2-[[(3-Aminophenyl)sulfanyl]methyl]-N-(cyanomethyl)cyclohexanecarboxamide 530108-71-5P, trans-N-(Cyanomethyl)-2-[[[3-(trifluoromethyl)phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530108-73-7P, 3-[[[trans-2-[[(Cyanomethyl)amino]carbonyl]cyclohexyl]methyl]sulfanyl]benzoic acid 530108-75-9P, 4-[[[trans-2-[[(Cyanomethyl)amino]carbonyl]cyclohexyl]methyl]sulfanyl]benzoic acid 530108-76-0P, trans-N-(Cyanomethyl)-2-[[(3-hydroxyphenyl)sulfanyl]methyl]cyclohexanecarboxamide 530108-78-2P, trans-N-(Cyanomethyl)-2-[[[3-(formylamino)phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530108-80-6P, trans-2-[[[3-(Acetylamino)phenyl]sulfanyl]methyl]-N-(cyanomethyl)cyclohexanecarboxamide 530108-82-8P, trans-2-[[[3-[Bis(methylsulfonyl)amino]phenyl]sulfanyl]methyl]-N-(cyanomethyl)cyclohexanecarboxamide 530108-84-0P, trans-N-(Cyanomethyl)-2-[[(4-iodophenyl)sulfanyl]methyl]cyclopentanecarboxamide 530108-86-2P, trans-N-(Cyanomethyl)-2-[[4-iodobenzenesulfonyl)methyl]cyclopentanecarboxamide 530108-88-4P, (1S/R,2R/S,3R/S,4R/S)-N-(Cyanomethyl)-3-[[(4-fluorophenyl)sulfanyl]methyl]bicyclo[2.2.1]hept-5-ene-2-carboxamide 530108-90-8P, (1R/S,2R/S,3R/S,4S/R)-N-(Cyanomethyl)-3-[[4-(methylsulfanyl)benzenesulfonyl]methyl]bicyclo[2.2.1]hept-5-ene-2-carboxamide 530108-92-0P, trans-N-(Cyanomethyl)-6-[[[4-(methylsulfanyl)benzene]sulfonyl]methyl]spiro[2.4]heptane-5-carboxamide 530108-94-2P, trans-N-(Cyanomethyl)-2-[(4-fluorobenzenesulfonyl)methyl]cyclopentanecarboxamide 530108-96-4P, trans-N-(Cyanomethyl)-2-[[4-(methylsulfanyl)benzenesulfonyl]methyl]cyclopentanecarboxamide 530108-98-6P, (1R/S,2R/S,3R/S,4S/R)-N-(Cyanomethyl)-3-[[(4-hydroxyphenyl)sulfanyl]methyl]bicyclo[2.2.1]hept-5-ene-2-carboxamide 530109-00-3P, (1R/S,2R/S,3R/S,4S/R)-N-(Cyanomethyl)-3-[[4-hydroxybenzenesulfonyl)methyl]bicyclo[2.2.1]hept-5-ene-2-carboxamide 530109-02-5P, N-(Cyanomethyl)-7-[(4-fluorobenzenesulfonyl)methyl]-3-oxatricyclo[3.2.1.02,4]octane-6-carboxamide 530109-04-7P, trans-N-(Cyanomethyl)-2-[[[(4-iodophenyl)sulfanyl]methyl]cyclohexanecarboxamide 530109-06-9P, trans-N-(Cyanomethyl)-2-[(4-iodobenzenesulfonyl)methyl]cyclohexanecarboxamide 530109-08-1P, trans-N-(Cyanomethyl)-2-[[[4-[(2,2,2-trifluoroethyl)sulfanyl]benzene]sulfonyl]methyl]cyclohexanecarboxamide 530109-10-5P, trans-N-(Cyanomethyl)-2-[[[4-[(difluoromethyl)sulfanyl]phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530109-12-7P, trans-N-(Cyanomethyl)-2-[[[4-[(difluoromethyl)sulfanyl]benzene]sulfonyl]methyl]cyclohexanecarboxamide 530109-14-9P, N-(Cyanomethyl)-2-[(4-fluorobenzenesulfonyl)methyl]-4-methylcyclopentanecarboxamide 530109-16-1P, N-(Cyanomethyl)-4-methyl-2-[[4-(methylsulfanyl)benzenesulfonyl]methyl]cyclopentanecarboxamide 530109-18-3P, N-(Cyanomethyl)-2-[(4-fluorobenzenesulfonyl)methyl]-5-methylcyclohexanecarboxamide 530109-20-7P, trans-N-(Cyanomethyl)-2-[(4-difluoromethoxybenzenesulfonyl)methyl]cyclohexanecarboxamide 530109-22-9P, trans-N-(Cyanomethyl)-2-[[4-(methylsulfanyl)phenoxy]methyl]cyclohexanecarboxamide 530109-24-1P, trans-2-[(4-Methoxybenzylsulfonyl)methyl]cyclohexanecarboxylic acid (cyanomethyl)amide 530109-27-4P, (1R/S,6R/S)-N-(Cyanomethyl)-6-[[[4-(methylsulfanyl)phenyl]sulfanyl]methyl]cyclohex-3-ene-1-carboxamide 530109-29-6P, trans-N-Cyanomethyl-2-[[[4-[(2-morpholinoethyl)oxy]phenyl]sulfanyl]methyl]cyclohexanecarboxamide 530109-33-2P, (1R/S,2S/R,3S/R,6S/R)-N-(Cyanomethyl)-3-[[(4-fluorophenyl)sulfanyl]methyl]bicyclo[4.1.0]heptane-2-carboxamide 530109-36-5P, (1R/S,2S/R,3S/R,6S/R)-N-(Cyanomethyl)-3-[[(4-fluorobenzene)sulfonyl]methyl]bicyclo[4.1.0]heptane-2-carboxamide 530109-38-7P, trans-N-Cyanomethyl-2-[[4-(4-((piperidin-4-yl)oxy)phenyl)benzenesulfonyl]methyl]cyclohexanecarboxamide 530109-40-1P, trans-N-Cyanomethyl-2-[[4-[[[[(4-dimethylaminophenyl)methyl]amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide trifluoroacetate 530109-42-3P, trans-N-Cyanomethyl-2-[[4-[[[[(2-(pyridin-4-yl)ethyl)amino]carbonyl]methyl]sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide trifluoroacetate 530109-44-5P, trans-N-Cyanomethyl-2-[[4-[(2-((pyridin-3-yl)oxy)ethyl)sulfanyl]benzenesulfonyl]methyl]cyclohexanecarboxamide trifluoroacetate 531500-29-5P, (1R/S,2R/S,3R/S,6S/R)-N-(Cyanomethyl)-3-[[[4-(methylsulfanyl)benzene]sulfonyl]methyl]bicyclo[4.1.0]heptane-2-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of aryl-contg. N-cyanoalkyl carboxamides as protease inhibitors)
RN 530104-19-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(phenylthio)methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



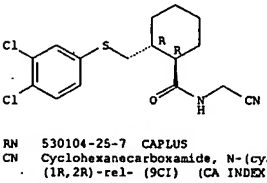
RN 530104-21-3 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(4-chlorophenyl)thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-23-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(3,4-dichlorophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

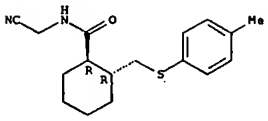
Relative stereochemistry.



RN 530104-25-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-methylphenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

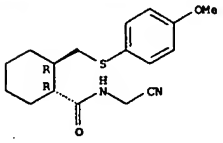
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



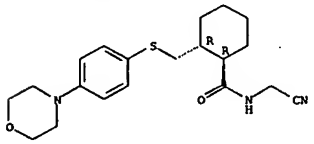
RN 530104-27-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[(4-methoxyphenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-28-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(4-morpholinyl)phenyl]thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

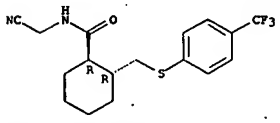
Relative stereochemistry.



RN 530104-30-4 CAPLUS
CN Cyclohexanecarboxamide, 2-[[[4-(acetylamino)phenyl]thio]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

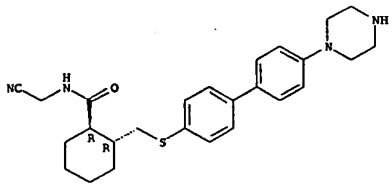
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



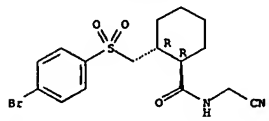
RN 530104-42-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-45-1 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(4-bromophenyl)sulfonyl]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

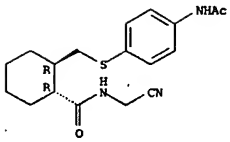
Relative stereochemistry.



RN 530104-47-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(4-morpholinyl)phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

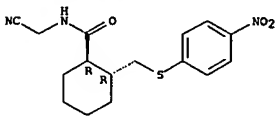
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



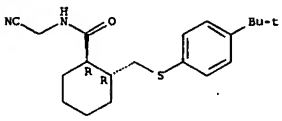
RN 530104-32-6 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-nitrophenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-34-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(1,1-dimethylethyl)phenyl]thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

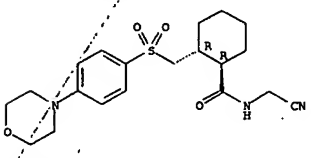
Relative stereochemistry.



RN 530104-36-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(trifluoromethyl)phenyl]thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

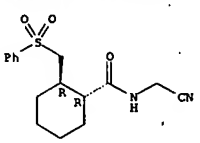
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



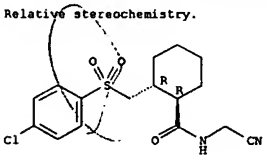
RN 530104-49-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[(phenylsulfonyl)methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-51-9 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(4-chlorophenyl)sulfonyl]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

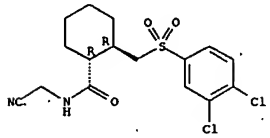
Relative stereochemistry.



RN 530104-53-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(3,4-dichlorophenyl)sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

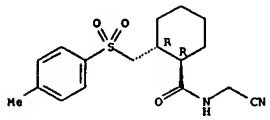
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



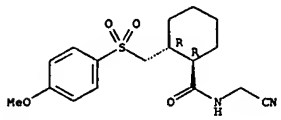
RN 530104-55-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-methylphenyl)sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-57-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-methoxyphenyl)sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

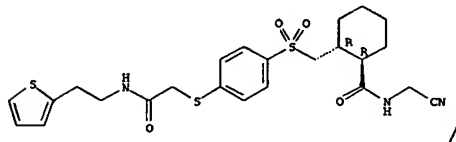
Relative stereochemistry.



RN 530104-59-7 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(4-bromophenyl)sulfinyl]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

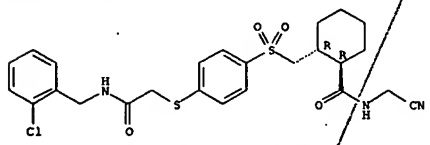
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



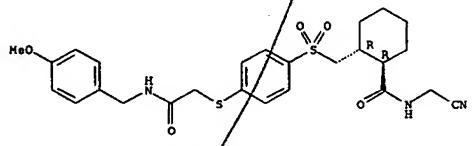
RN 530104-71-3 CAPLUS
CN Cyclohexanecarboxamide, 2-[[[4-[[2-[[(2-chlorophenyl)methyl]amino]-2-oxoethyl]thio]phenyl]sulfonyl]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-73-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-[[(4-methoxyphenyl)methyl]amino]-2-oxoethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

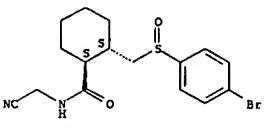
Relative stereochemistry.



RN 530104-74-6 CAPLUS
CN Cyclohexanecarboxamide, 2-[[[4-[[2-[[(4-chlorophenyl)methyl]amino]-2-oxoethyl]thio]phenyl]sulfonyl]methyl]-N-(cyanomethyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

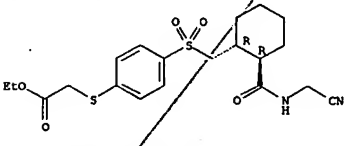
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



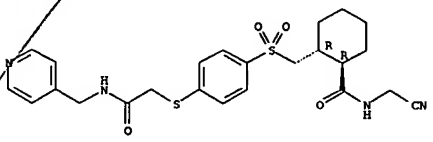
RN 530104-61-1 CAPLUS
CN Acetic acid, [[4-[[[(1R,2R)-2-[[(cyanomethyl)amino]carbonyl]cyclohexyl]methyl]sulfonyl]phenyl]thio]-, ethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-67-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-oxo-2-[(4-pyridinylmethyl)amino]ethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

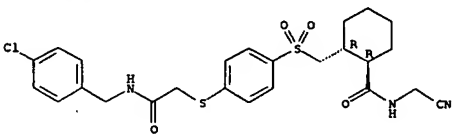
Relative stereochemistry.



RN 530104-69-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-oxo-2-[[2-(2-thienyl)ethyl]amino]ethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

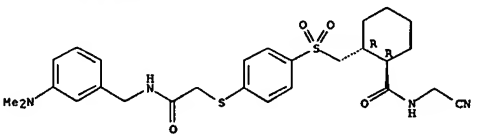
Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



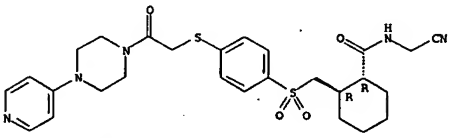
RN 530104-76-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-[[[3-(dimethylamino)phenyl]methyl]amino]-2-oxoethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-78-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-oxo-2-[4-(4-pyridinyl)-1-piperazinyl]ethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

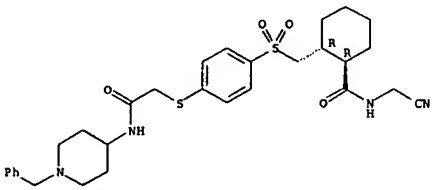


RN 530104-80-4 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-oxo-2-[[1-(phenylmethyl)-4-piperidinyl]amino]ethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

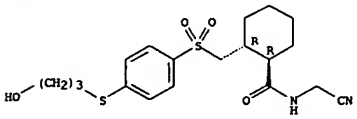
Karen Cheng

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



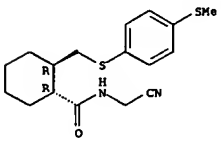
RN 530104-84-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[(3-hydroxypropyl)thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



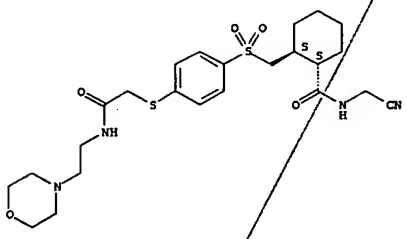
RN 530104-86-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-(methylthio)phenyl]thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-88-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[(4-hydroxyphenyl)thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

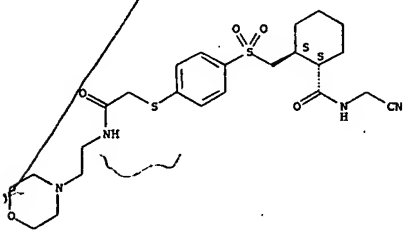


RN 530105-00-1 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-[(2-(4-morpholinyl)ethyl]amino]-2-oxoethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 530104-99-5
CMF C24 H34 N4 O5 S2

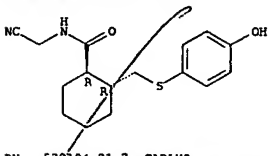
Relative stereochemistry.



CM 2

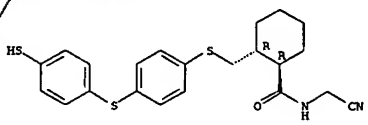
CRN 76-05-1
CMF C2 H F3 O2

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Relative stereochemistry.



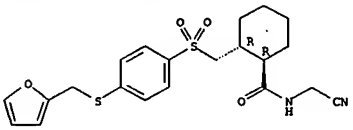
RN 530104-91-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[(4-mercaptophenyl)thio]phenyl]thio]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-96-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[(2-furanylmethyl)thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 530104-99-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-[[2-(4-morpholinyl)ethyl]amino]-2-oxoethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

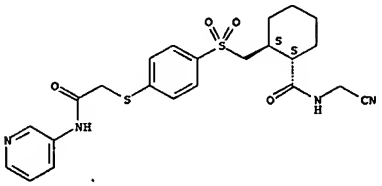
L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 530105-06-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-oxo-2-(3-pyridinylamino)ethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 530105-05-6
CMF C23 H26 N4 O4 S2

Relative stereochemistry.



CM 2

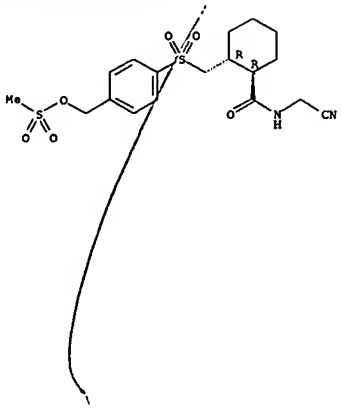
CRN 76-05-1
CMF C2 H F3 O2

RN 530105-10-3 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-2-[[[4-[[2-[4-(1-methylethyl)-1-piperazinyl]-2-oxoethyl]thio]phenyl]sulfonyl]methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

L11 ANSWER 35 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(CA INDEX NAME)

Relative stereochemistry.



L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:964345 CAPLUS
DOCUMENT NUMBER: 138:24952
TITLE: Preparation of novel amino nitriles useful as reversible inhibitors of cysteine proteases
INVENTOR(S): Hickey, Eugene R.; Bekkali, Younes; Patel, Usha R.; Spero, Denice M.; Thomson, David S.; Young, Erick R. R.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 223 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100849	A2	20021219	WO 2002-US17590	20020605
WO 2002100849	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003119827	A1	20030626	US 2002-163015	20020604
US 6982263	B2	20060103		
CA 2449192	A1	20021219	CA 2002-2449192	20020605
AU 2002314898	A1	20021223	AU 2002-314898	20020605
EP 1399431	A2	20040324	EP 2002-741825	20020605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005501017	T	20050113	JP 2003-503617	20020605
PRIORITY APPLN. INFO.:			US 2001-296863P	P 20010608
			WO 2002-US17590	W 20020605

OTHER SOURCE(S): MARPAT 138:24952

AB Novel nitrile compds. YCO2CR2R3C(:X)NR6CR4R5CN [Y = R1, R1O, R1S, R12N, R13C, where R1 = H, (un)substituted (cyclo)alkyl, aryl, benzyl, tetrahydronaphthyl, indenyl, indanyl, alkylsulfonylalkyl, cycloalkylsulfonylalkyl, arylsulfonylalkyl, heterocyclyl, or heteroaryl; R2-R5 = H, (un)substituted (cyclo)alkyl, aryl, etc. or CR2R3 and CR4R5 may form rings; R6 = H, OH, or (cyclo)alkyl; X = O or S (with provisos)] or their pharmaceutically-acceptable derivs. were prepared as reversible inhibitors of cysteine proteases such as cathepsin K, S, F, L and B for treating diseases and pathol. conditions exacerbated by these proteases such as osteoporosis, rheumatoid arthritis, multiple sclerosis, asthma and other autoimmune diseases, Alzheimer's disease, and atherosclerosis. Thus, morpholine-4-carboxylic acid 1-[[(benzyloxymethyl)cyanomethyl]carbamoyl]-3-methylbutyl ester was prepared from N-(tert-butoxycarbonyl)-O-benzyl-L-serine, 2-Hydroxyisocaproic acid, and 4-morpholinecarbonyl chloride.

IT 478279-63-9P 478279-64-0P 478279-65-1P

L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

478279-67-3P 478279-68-4P 478279-69-5P
478279-74-2P 478279-75-3P 478279-76-4P
478279-77-5P 478279-78-6P 478279-79-7P
478279-86-6P 478279-87-7P 478279-88-8P
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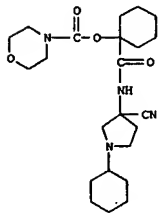
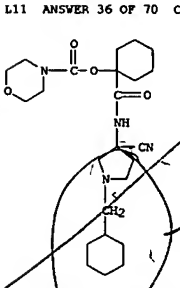
478279-92-4P 478279-93-5P 478279-95-7P
478280-08-9P 478280-09-0P 478280-10-3P
478280-17-0P 478280-18-1P 478280-19-2P
478280-25-0P 478280-32-9P 478280-33-0P
478280-39-6P 478280-40-9P 478280-41-0P
478280-48-7P 478280-49-8P 478280-50-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel amino nitriles as reversible inhibitors of cysteine proteases)

RN 478279-63-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-cyclohexyl-3-pyrrolidinyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

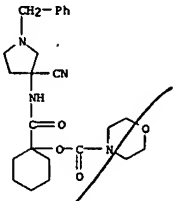


RN 478279-64-0 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-(cyclohexylmethyl)-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

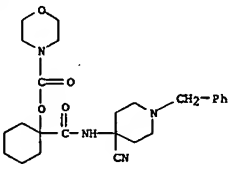
L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 478279-65-1 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(3-cyano-1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

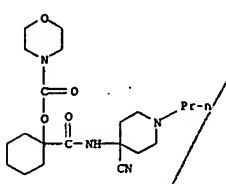


RN 478279-67-3 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-(phenylmethyl)-4-piperidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

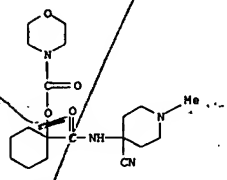


L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

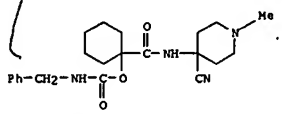
RN 478279-68-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)



RN 478279-69-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

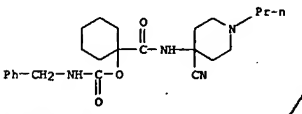


RN 478279-74-2 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

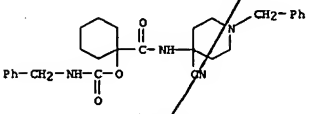


RN 478279-75-3 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[(4-cyano-1-propyl-4-

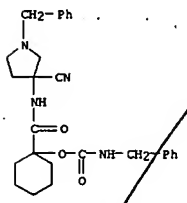
L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
piperidinyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)



RN 478279-76-4 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[[4-cyano-1-(phenylmethyl)-4-piperidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

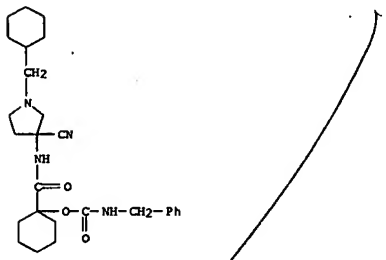


RN 478279-77-5 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[[3-cyano-1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

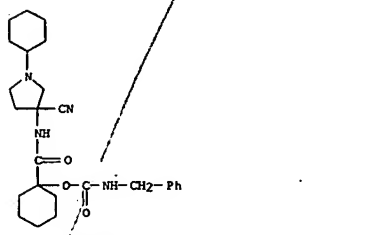


RN 478279-78-6 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[[3-cyano-1-(cyclohexylmethyl)-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

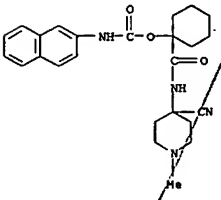


RN 478279-79-7 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[[3-cyano-1-cyclohexyl-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

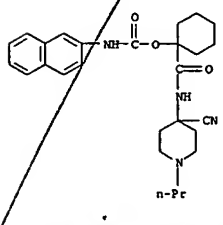


RN 478279-86-6 CAPLUS
CN Carbamic acid, 2-naphthalenyl-, 1-[[(4-cyano-1-methyl-4-piperidinyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

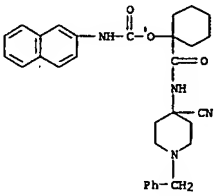
L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



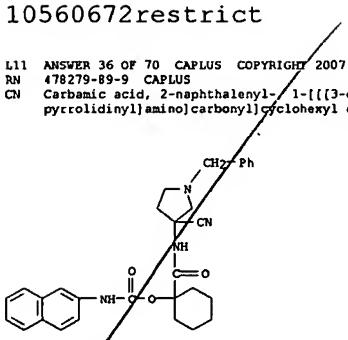
RN 478279-87-7 CAPLUS
CN Carbamic acid, 2-naphthalenyl-, 1-[[(4-cyano-1-propyl-4-piperidinyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)



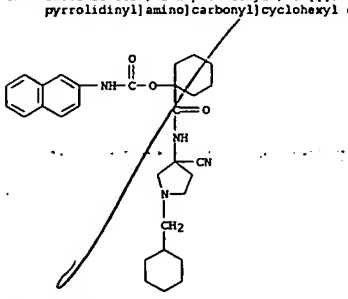
RN 478279-88-8 CAPLUS
CN Carbamic acid, 2-naphthalenyl-, 1-[[[4-cyano-1-(phenylmethyl)-4-piperidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)



L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 478279-89-9 CAPLUS
CN Carbamic acid, 2-naphthalenyl-, 1-[[[3-cyano-1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

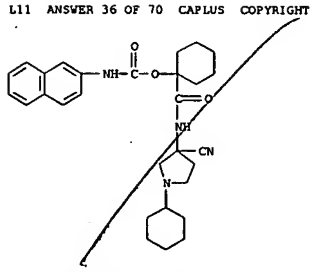


RN 478279-90-2 CAPLUS
CN Carbamic acid, 2-naphthalenyl-, 1-[[[3-cyano-1-(cyclohexylmethyl)-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

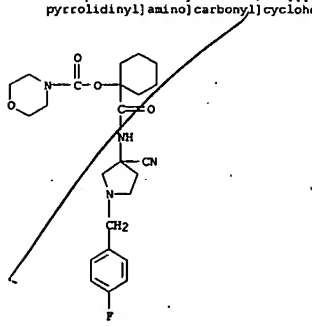


RN 478279-91-3 CAPLUS
CN Carbamic acid, 2-naphthalenyl-, 1-[[(3-cyano-1-cyclohexyl-3-pyrrolidinyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

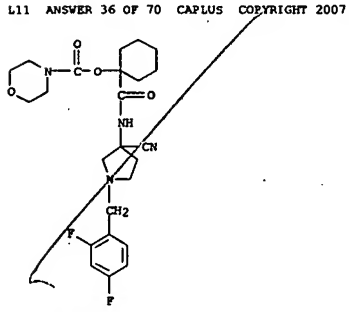


RN 478279-92-4 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[3-cyano-1-[(4-fluorophenyl)methyl]-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

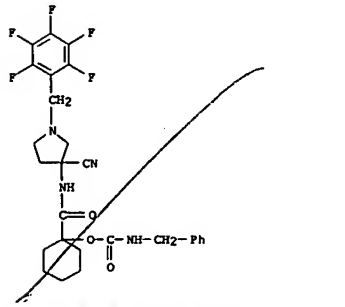


RN 478279-93-5 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[3-cyano-1-[(2,4-difluorophenyl)methyl]-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

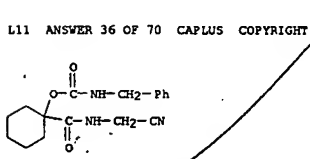


RN 478279-95-7 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[[3-cyano-1-[(pentafluorophenyl)methyl]-3-pyrrolidinyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

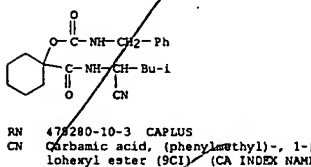


RN 478280-08-9 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[(cyanomethyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

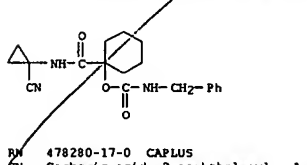
L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 478280-09-0 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[(1-cyano-3-methylbutyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

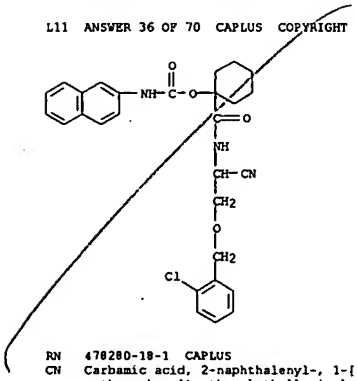


RN 478280-10-3 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[(1-cyanocyclopropyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

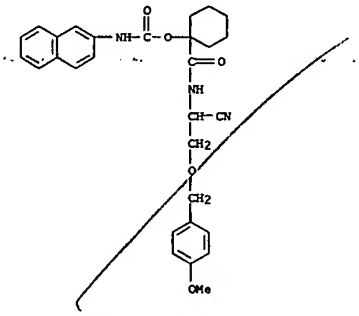


RN 478280-17-0 CAPLUS
CN Carbamic acid, 2-naphthalenyl-, 1-[[[2-[(2-chlorophenyl)methoxy]-1-cyanoethyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

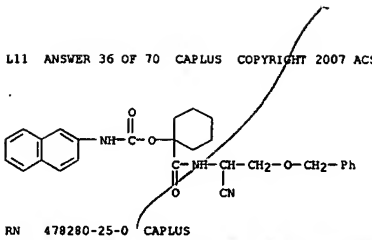


RN 478280-18-1 CAPLUS
CN Carbamic acid, 2-naphthalenyl-, 1-[[[1-cyano-2-[(4-methoxyphenyl)methoxy]ethyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

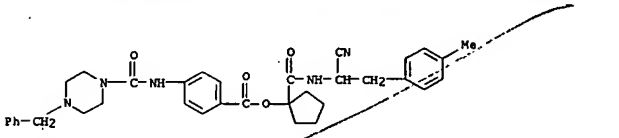


RN 478280-19-2 CAPLUS
CN Carbamic acid, 2-naphthalenyl-, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

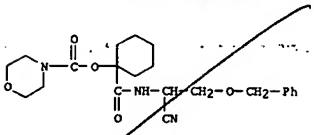
L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



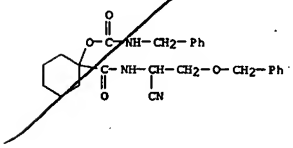
RN 478280-25-0 CAPLUS
CN Benzoic acid, 4-[[[4-(phenylmethyl)-1-piperazinyl]carbonyl]amino]-, 1-[[[1-cyano-2-(4-methylphenyl)ethyl]amino]carbonyl]cyclopentyl ester (9CI) (CA INDEX NAME)



RN 478280-32-9 CAPLUS
CN 4-Morpholinecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

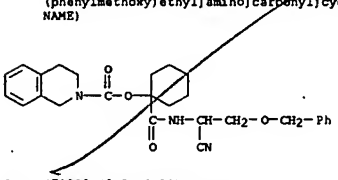


RN 478280-33-0 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

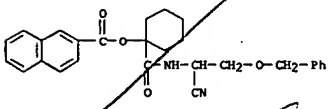


L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

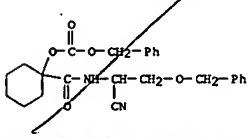
RN 478280-39-6 CAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)



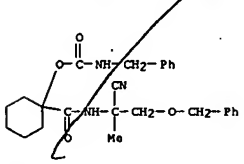
RN 478280-40-9 CAPLUS
CN 2-Naphthalenecarboxylic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)



RN 478280-41-0 CAPLUS
CN Carbonic acid, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl phenylmethyl ester (9CI) (CA INDEX NAME)

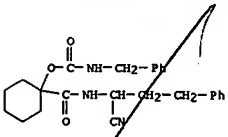


RN 478280-48-7 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[[1-cyano-1-methyl-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)

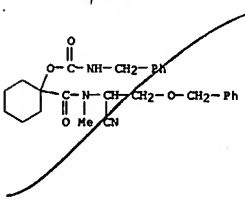


L11 ANSWER 36 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 478280-49-8 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[(1-cyano-3-phenylpropyl)amino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)



RN 478280-50-1 CAPLUS
CN Carbamic acid, (phenylmethyl)-, 1-[[[1-cyano-2-(phenylmethoxy)ethyl]methylamino]carbonyl]cyclohexyl ester (9CI) (CA INDEX NAME)



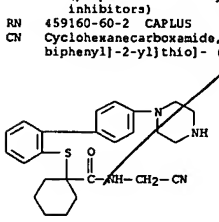
Karen Cheng

L11 ANSWER 37 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:695723 CAPLUS
DOCUMENT NUMBER: 137:232908
TITLE: Preparation of N-cyanomethyl amides as cathepsin cysteine protease inhibitors
INVENTOR(S): Prasit, Petpiboon; Bayly, Christopher Ian; Robichaud, Joel Stephane; Black, W. Cameron; Setti, Eduardo L.; Rydzewski, Robert M.; Palmer, James T.
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.; PE Corporation (NY); AXYS Pharm. Inc.
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

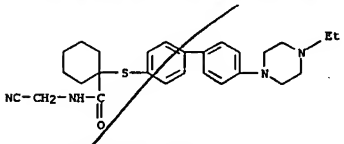
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069901	A2	20020912	WO 2002-US6533	20020301
WO 2002069901	A3	20031030		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2439415	A1	20020912	CA 2002-2439415	20020301
AU 2002254099	A1	20020919	AU 2002-254099	20020301
EP 1372655	A2	20040102	EP 2002-723314	20020301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004531486	T	20041014	JP 2002-569079	20020301
US 2004198982	A1	20041007	US 2003-469430	20030828
US 7012075	B2	20060314		
PRIORITY APPLN. INFO.:			US 2001-272799P	P 20010302
			WO 2002-US6533	W 20020301

OTHER SOURCE(S): MARPAT 137:232908
AB The invention relates to a novel class of compds. R5-(E)n-D-X-CR3R4CONHCR1R2CN [R1 = H, (halo)alkyl, or (halo)alkenyl or R1R2C is a cycloalkyl ring optionally substituted by alkyl, hydroxyalkyl, or halogen; R3, R4 = H, alkyl or alkenyl optionally substituted by cycloalkyl or halogen or R3R4C is cycloalkyl, cycloalkenyl or heterocyclyl optionally substituted by alkyl, halo, hydroxyalkyl, hydroxy, alkoxy, or keto; X = NH, NR6, NHSO2, O, CR7R8O, OCR7R8, CR7R8CR7R8O, S, SO2, CR7R8S, SCR7R8, CR7R8SO2, SO2CR7R8, CR7R8, CR7R8NR7, NR7CR7R8, where R6 = alkyl or R6 and R4 form a 4-12 membered heterocyclyl ring system which is optionally substituted and R7, R8 = H or alkyl; D, E = (un)substituted aryl, heteroaryl, cycloalkyl, or heterocyclyl; n = 1-2; R5 = H, alkyl, alkenyl, alkoxy, halo, nitro, cyano, amino, aryl, heteroaryl, cycloalkyl, heterocyclyl, CO2H, OH, alkoxy, SH, sulfonyl groups, etc.] and their pharmaceutically-acceptable salts and N-oxide derivs. are cysteine

L11 ANSWER 37 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
protease inhibitors and are useful for treating diseases in which inhibition of bone resorption is indicated, such as osteoporosis. Thus, C4H9N2-p-C6H4-p-C6H4-L-Leu-NHCH2CN (C4H9N2 = 1-piperazinyl) was prepd. from L-leucine, 1,4-dibromobenzene, aminoacetonitrile hydrochloride, and 4-[4-(tert-butoxycarbonyl)-1-piperazinyl]phenylboronic acid (prepn. given). The product was used to prep. a pharmaceutical compn.
IT 459160-60-2P 459161-54-7P 459162-03-9P
459162-47-1P 459162-59-5P 459162-62-0P
459162-63-1P 459162-64-2P 459162-67-5P
459162-69-7P 459164-49-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-cyanomethyl amides as cathepsin cysteine protease inhibitors)
RN 459160-60-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[[4'-(1-piperazinyl)[1,1'-biphenyl]-2-yl]thio]- (9CI) (CA INDEX NAME)

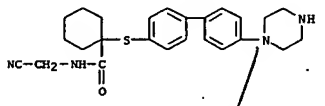


RN 459161-54-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[[4'-(4-ethyl-1-piperazinyl)[1,1'-biphenyl]-4-yl]thio]- (9CI) (CA INDEX NAME)

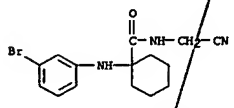


RN 459162-03-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]thio]- (9CI) (CA INDEX NAME)

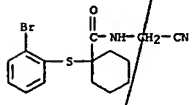
L11 ANSWER 37 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



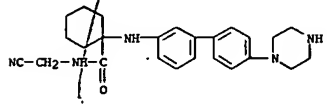
RN 459162-47-1 CAPLUS
CN Cyclohexanecarboxamide, 1-[(3-bromophenyl)amino]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



RN 459162-59-5 CAPLUS
CN Cyclohexanecarboxamide, 1-[(2-bromophenyl)thio]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

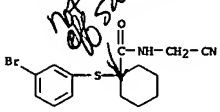


RN 459162-62-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[[4'-(1-piperazinyl)[1,1'-biphenyl]-3-yl]amino]- (9CI) (CA INDEX NAME)

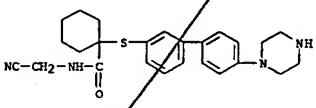


RN 459162-63-1 CAPLUS
CN Cyclohexanecarboxamide, 1-[(3-bromophenyl)thio]-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

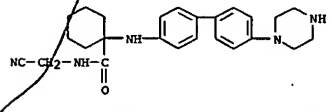
L11 ANSWER 37 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



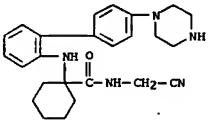
RN 459162-64-2 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[[4'-(1-piperazinyl)[1,1'-biphenyl]-3-yl]thio]- (9CI) (CA INDEX NAME)



RN 459162-67-5 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]amino]- (9CI) (CA INDEX NAME)



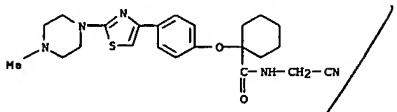
RN 459162-69-7 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[[4'-(1-piperazinyl)[1,1'-biphenyl]-2-yl]amino]- (9CI) (CA INDEX NAME)

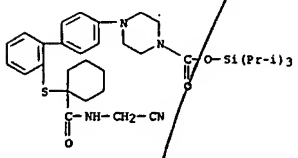


RN 459164-49-9 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)-1-[4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]phenoxy]- (9CI) (CA INDEX NAME)

Karen Cheng

L11 ANSWER 37 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)





IT 459164-76-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-cyanomethyl amides as cathepsin cysteine protease inhibitors)
RN 459164-76-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[2'-[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]thio][1,1'-biphenyl]-4-yl]-, tris(1-methylethyl)silyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:923748 CAPLUS
DOCUMENT NUMBER: 136:53544
TITLE: β-amino acid nitrile derivs. useful for the treatment of diseases which are associated with cysteine proteases
INVENTOR(S): Gabriel, Tobias; Pech, Michael; Rodriguez Sarmiento, Rosa Maria
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

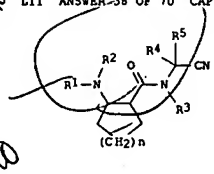
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001096285	A1	20011220	WO 2001-EP6541	20010608
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002016361	A1	20020207	US 2001-872927	20010601
US 6462076	B2	20021008		
CA 2410303	A1	20011220	CA 2001-2410303	20010608
EP 1294679	A1	20030326	EP 2001-943489	20010608
EP 1294679	B1	20050921		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL; TR				
BR 2001011733	A	20030527	BR 2001-11733	20010608
HU 200300896	A2	20030728	HU 2003-896	20010608
JP 2004503525	T	20040205	JP 2002-510429	20010608
JP 3872427	B2	20070124		
NZ 522587	A	20040730	NZ 2001-522587	20010608
RU 2245871	C2	20050210	RU 2002-135634	20010608
AT 304997	T	20051015	AT 2001-943489	20010608
ES 2248346	T3	20060316	ES 2001-1943489	20010608
ZA 2002009415	A	20040219	ZA 2002-9415	20021119
NO 2002005823	A	20021204	NO 2002-5823	20021204
IN 2002CN02031	A	20050225	IN 2002-CN2031	20021210
MX 2002PA12253	A	20030425	MX 2002-PA12253	20021211
PRIORITY APPLN. INFO.:			EP 2000-112577 A	20000614
			WO 2001-EP6541 W	20010608

OTHER SOURCE(S): MARPAT 136:53544
GI

no amido

amido

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



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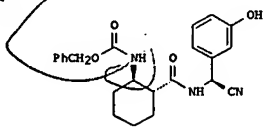
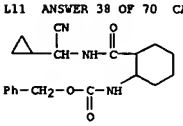


II

AB Compds. of formula I (R1 = H, aryl, C(O)Ra, or SO2Rb (Ra = lower alkyl, lower-alkoxy, cycloalkyl, cycloalkyl-lower-alkyl, cycloalkyl-lower alkoxy, cycloalkoxy, aryl, aryloxy, etc.; Rb = aryl, acyl-lower-alkyl, or heteroaryl); R2, R3, R4 = H or lower-alkyl; R5 = H, lower-alkyl, cycloalkyl, or aryl; n = 1,2) were prepared. Thus, (1R,2R)-(2-((S)-(cyano(3-hydroxyphenyl)methyl]carbamoyl)cyclohexyl)carbamic acid benzyl ester (II) was produced from (1R,2R)-2-benzyloxycarbonylaminocyclohexane carboxylic acid and (S)-2-amino-2-(3-hydroxyphenyl)acetonitrile. II was assayed against cathepsins K, S, L, and B and the inhibitory activity (IC50) was determined to be 0.005, >10, 4.7, and 4.6 μMol/L, resp. The compds. and pharmaceutically acceptable salts and/or pharmaceutically acceptable esters thereof are useful for the treatment of diseases which are associated with cysteine proteases such as osteoporosis, osteoarthritis, rheumatoid arthritis, tumor metastasis, glomerulonephritis, atherosclerosis, myocardial infarction, angina pectoris, instable angina pectoris, stroke, plaque rupture, transient ischemic attacks, amaurosis fugax, peripheral arterial occlusive disease, restenosis after angioplasty and stent placement, abdominal aortic aneurysm formation, inflammation, autoimmune disease, malaria, ocular fundus tissue cytopathy and respiratory disease. A discussion of pharmaceutical compns. is also included.

IT 381241-01-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of beta-amino acid nitrile derivs. useful for the treatment of diseases which are associated with cysteine proteases)
RN 381241-01-6 CAPLUS
CN Carbamic acid, [2-[[(cyanocyclopropylmethyl)amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



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381239-31-2P 381239-33-4P 381239-35-6P
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381240-65-9P 381240-66-0P 381240-67-1P
381240-68-2P 381240-69-3P 381240-70-6P
381240-71-7P 381240-72-8P 381240-73-9P
381240-74-0P 381240-75-1P 381240-76-2P
381240-77-3P 381240-79-5P 381240-80-8P
381240-81-9P 381240-82-0P 381240-83-1P
381240-84-2P 381240-85-3P 381240-86-4P
381240-87-5P 381240-88-6P 381240-89-7P

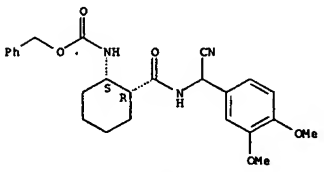
Karen Cheng

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

381240-90-0P 381240-91-1P 381240-92-2P
381240-93-3P 381240-94-4P 381240-95-5P
381240-96-6P 381240-97-7P 381240-98-8P
381240-99-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of beta-amino acid nitrile derivs. useful for the treatment of diseases which are assocd. with cysteine proteases)

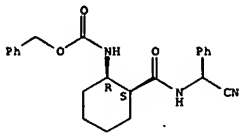
RN 381239-09-4 CAPLUS
CN Carbamic acid, [(1R,2S)-2-[[[cyano(3,4-dimethoxyphenyl)methyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 381239-10-7 CAPLUS
CN Carbamic acid, [(1R,2S)-2-[[(cyanophenylmethyl)amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

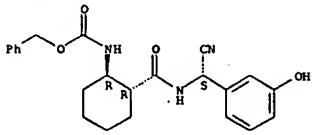


RN 381239-12-9 CAPLUS
CN Cyclohexanecarboxamide, 2-[[(4-chlorophenyl)sulfonyl]amino]-N-[cyano(3-hydroxyphenyl)methyl]-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

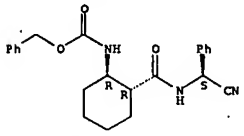
L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.



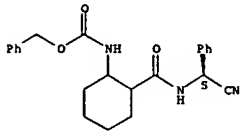
RN 381239-22-1 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[[(S)-cyanophenylmethyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 381239-24-3 CAPLUS
CN Carbamic acid, [2-[[[(S)-cyanophenylmethyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

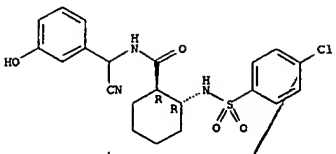
Absolute stereochemistry.



RN 381239-26-5 CAPLUS
CN Carbamic acid, [(1R,2S)-2-[[[cyano(2,4-dimethoxyphenyl)methyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester, rel- (9CI) (CA INDEX NAME)

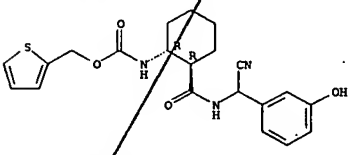
Relative stereochemistry.

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



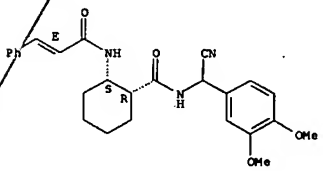
RN 381239-15-2 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[[cyano(3-hydroxyphenyl)methyl]amino]carbonyl]cyclohexyl]-, 2-thienylmethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



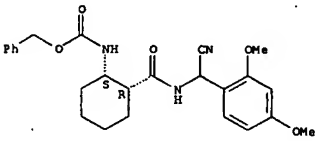
RN 381239-17-4 CAPLUS
CN Cyclohexanecarboxamide, N-[cyano(3,4-dimethoxyphenyl)methyl]-2-[[(2E)-1-oxo-3-phenyl-2-propenyl]amino]-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



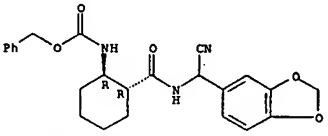
RN 381239-19-6 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[[(S)-cyano(3-hydroxyphenyl)methyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



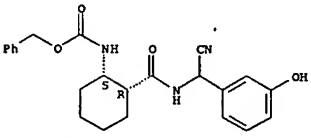
RN 381239-27-6 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[(1,3-benzodioxol-5-ylcyanomethyl)amino]carbonyl]cyclohexyl]-, phenylmethyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 381239-29-8 CAPLUS
CN Carbamic acid, [(1R,2S)-2-[[[cyano(3-hydroxyphenyl)methyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester, rel- (9CI) (CA INDEX NAME)

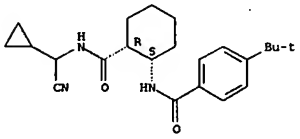
Relative stereochemistry.



RN 381239-30-1 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[[cyano(3-hydroxyphenyl)methyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester, rel- (9CI) (CA INDEX NAME)

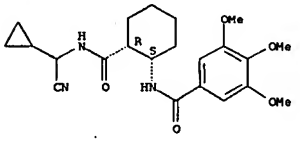
Relative stereochemistry.

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 381240-99-9 CAPLUS
CN Benzamide, N-[(1R,2S)-2-[[(cyanocyclopropylmethyl)amino]carbonyl]cyclohexyl]-3,4,5-trimethoxy-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 381241-15-2 381241-18-5 381242-00-8
381242-06-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of beta-amino acid nitrile derivs. useful for the treatment of
diseases which are associated with cysteine proteases)
RN 381241-15-2 CAPLUS
CN Cyclohexanecarboxamide, 2-amino-N-[cyano(3,4-dimethoxyphenyl)methyl]-, (1R,2S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

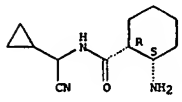
CRN 381241-14-1
CMF C17 H23 N3 O3

Relative stereochemistry.

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 381242-00-8 CAPLUS
CN Cyclohexanecarboxamide, 2-amino-N-(cyanocyclopropylmethyl)-, (1R,2S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

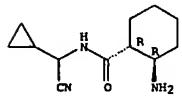


RN 381242-06-4 CAPLUS
CN Cyclohexanecarboxamide, 2-amino-N-(cyanocyclopropylmethyl)-, (1R,2R)-rel-, monoacetate (9CI) (CA INDEX NAME)

CM 1

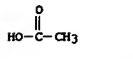
CRN 381242-05-3
CMF C12 H19 N3 O

Relative stereochemistry.



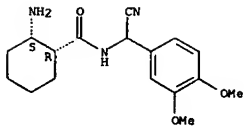
CM 2

CRN 64-19-7
CMF C2 H4 O2



IT 381241-04-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of beta-amino acid nitrile derivs. useful for the treatment of

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



CM 2

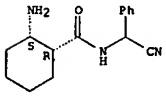
CRN 76-05-1
CMF C2 H F3 O2

RN 381241-18-5 CAPLUS
CN Cyclohexanecarboxamide, 2-amino-N-(cyanophenylmethyl)-, (1R,2S)-rel-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 381241-17-4
CMF C15 H19 N3 O

Relative stereochemistry.



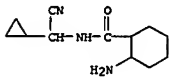
CM 2

CRN 76-05-1
CMF C2 H F3 O2

L11 ANSWER 38 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
diseases which are assocd. with cysteine proteases)
RN 381241-04-9 CAPLUS
CN Cyclohexanecarboxamide, 2-amino-N-(cyanocyclopropylmethyl)-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 381241-03-8
CMF C12 H19 N3 O



CM 2

CRN 64-19-7
CMF C2 H4 O2

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10560672restrict

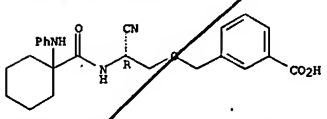
L11 ANSWER 39 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:851106 CAPLUS
DOCUMENT NUMBER: 135:371998
TITLE: Preparation of N-substituted peptidyl nitriles as cysteine cathepsin inhibitors
INVENTOR(S): Cowen, Scott Douglas; Greenspan, Paul David; McQuire, Leslie Wighton; Tommasi, Ruben Alberto; Van Duzer, John Henry
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087828	A1	20011122	WO 2001-EP5463	20010514
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2407463	A1	20011122	CA 2001-2407463	20010514
EP 1283825	A1	20030219	EP 2001-977958	20010514
EP 1283825	B1	20050914		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003533506	T	20031111	JP 2001-584225	20010514
AT 304526	T	20050915	AT 2001-977958	20010514
ES 2249482	T3	20060401	ES 2001-1977958	20010514
US 2003158256	A1	20030821	US 2002-275583	20021107
US 6812237	B2	20041102		
PRIORITY APPLN. INFO.:			US 2000-204217P	P 20000515
			WO 2001-EP5463	W 20010514

OTHER SOURCE(S): MARPAT 135:371998
AB Peptidyl nitriles R1NHCR2R3CONHCR4R5CN [R1 is (bi)aryl; R2 is (bi)aryl-lower alkyl, benzo-fused cycloalkyl, (bi)cycloalkyl-lower alkyl, aryloxy-lower alkyl, or aryl-C2-C7-alkyl in which C2-C7-alkyl is interrupted by Y (Y is O, S, SO, SO2, CO, NH or alkylimino); R3 is H or lower alkyl or R2 and R3 combined are C2-C7-alkylene or -alkylene interrupted by Y; R4 is H or lower alkyl; R5 is H, optionally substituted lower alkyl, (bi)aryl-lower alkyl, (bi)cycloalkyl-lower alkyl, aryloxy-lower alkyl, or aryl-C2-C7-alkyl in which C2-C7-alkyl is interrupted by Y] or their pharmaceutically acceptable salts were prepared as cysteine cathepsin inhibitors. Thus, N-[2-(3-carboxy-4-fluorobenzyloxy)-1(S)-cyanoethyl]-3-methyl-Nα-phenyl-L-phenylalaninamide was prepared by condensation of (S)-2-amino-3-[3-[[2-(trimethylsilyl)ethoxy]carbonyl]-4-fluorobenzyloxy]propionitrile with Nα-phenyl-3-methyl-L-phenylalanine (syntheses given), followed by

L11 ANSWER 39 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
ester cleavage.
IT 374119-63-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-substituted peptidyl nitriles as cysteine cathepsin inhibitors)
RN 374119-63-8 CAPLUS
CN Benzoic acid, 3-[[(2R)-2-cyano-2-[[[1-(phenylamino)cyclohexyl]carbonyl]amino]ethoxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

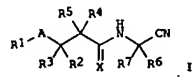


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

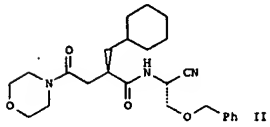
L11 ANSWER 40 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:833854 CAPLUS
DOCUMENT NUMBER: 135:371749
TITLE: Preparation of succinic acid diamides as cysteine protease inhibitors
INVENTOR(S): Bekkali, Younes; Betageri, Rajashekar; Emmanuel, Michel Jose; Hickey, Eugene Richard; Liu, Weimin; Patel, Usha R.; Spero, Denice Mary; Thomson, David S.; Ward, Yancey David; Young, Erick Richard Roush
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 75 pp., Cont.-in-part of U.S. Ser. No. 627,869.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001041700	A1	20011115	US 2001-862674	20010522
US 6313117	B1	20011106	US 2000-627869	20000728
US 2003087939	A1	20030508	US 2002-278546	20021023
US 6649642	B2	20031118		
PRIORITY APPLN. INFO.:			US 1999-146647P	P 19990730
			US 2000-627869	A2 20000728
			US 2001-862674	A1 20010522

OTHER SOURCE(S): MARPAT 135:371749
GI



I

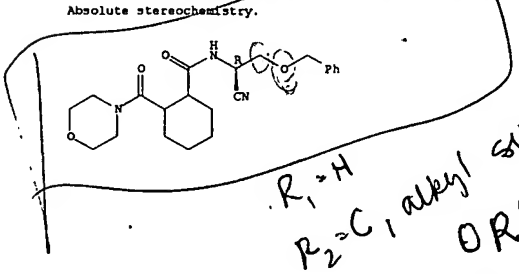


II

AB Title compds. [I; A = CO, R8OCH; R1 = (substituted) alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, amino; R2 = H, alkyl, OH, alkoxy; R3, R4 = H, alkyl; R5 = H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl; R6 = H, alkyl optionally interrupted by 1-2 N, O, S; R7 = H, alkyl, alkyl interrupted by 1-2 N, O, S, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl, cyano; R6R7 = atoms to form a 4-7 membered heterocyclic or carbocyclic ring; R8 = H, alkyl, cycloalkyl, cycloalkylalkyl, aralkyl; X =

L11 ANSWER 40 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
O, S), were prepd. as inhibitors of cysteine proteases such as cathepsins B, F, K, L, and S in the treatment of autoimmune diseases, Alzheimer's disease, and atherosclerosis. Thus, (R)-2-cyclohexylmethyl-4-morpholin-4-yl-4-oxobutyric acid (prepn. given) in DMF at 0° was treated with EDC, 1-hydroxybenzotriazole, O-benzyl-L-serinamide.HCl, and N-methylmorpholine followed by stirring overnight to give N-(2-benzyloxy-1-carbamoylethyl)-2-cyclohexylmethyl-4-morpholin-4-yloxobutyramide. The latter was stirred 1 h with cyanuric chloride in DMF at 0° to give title compd. (II). I inhibited cathepsin S with IC50≤ 100 μM.
IT 324795-10-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of succinic acid diamides as inhibitors of cysteine proteases
(cathepsins) in the treatment of autoimmune diseases, Alzheimer's disease, and atherosclerosis)
RN 324795-10-0 CAPLUS
CN Cyclohexanecarboxamide, N-[(1R)-1-cyano-2-(phenylmethoxy)ethyl]-2-(4-morpholinylcarbonyl)- (9CI) (CA INDEX NAME)

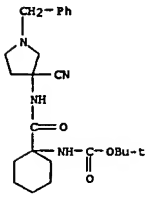
Absolute stereochemistry.



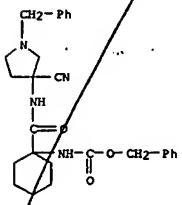
R_1 = H
R_2 = C, alkyl subst. w/ OR^6...
R^6 = C, alkyl aryl
n = 2
p = 0
D = C, alkyl subst. w/ KOO.
E = heterocycl
R5 = H

Karen Cheng

L11 ANSWER 43 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
cysteine proteases)
RN 331280-90-1 CAPLUS
CN Carbamic acid, [1-[[[3-cyano-1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]cyclohexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 331280-92-3 CAPLUS
CN Carbamic acid, [1-[[[3-cyano-1-(phenylmethyl)-3-pyrrolidinyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



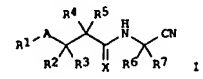
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 44 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:101117 CAPLUS
DOCUMENT NUMBER: 134:163044
TITLE: Preparation of succinic acid diamides as cysteine protease inhibitors
INVENTOR(S): Bekkali, Younes; Betageri, Raj; Emmanuel, Michel; Hickey, Eugene; Liu, Weimin; Spero, Denice M.; Thomson, David S.; Ward, Yancey; Young, Erick R. R.; Patel, Usha
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

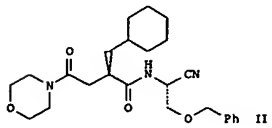
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009110	A1	20010208	WO 2000-US20453	20000728
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2379747	A1	20010208	CA 2000-2379747	20000728
EP 1204652	A1	20020515	EP 2000-950777	20000728
EP 1204652	B1	20060517		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506364	T	20030218	JP 2001-514313	20000728
AT 326454	T	20060615	AT 2000-950777	20000728
MX 2002PA01014	A	20020812	MX 2002-PA1014	20020129
PRIORITY APPLN. INFO.:			US 1999-146647P P	19990730
			WO 2000-US20453 W	20000728

OTHER SOURCE(S): MARPAT 134:163044
GI

L11 ANSWER 44 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I

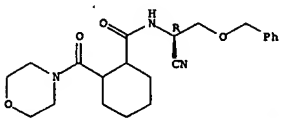


II

AB Title compds. [I; A = CO, R8OCH; R1 = (substituted) alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, amino; R2 = H, alkyl, OH, alkoxy; R3, R4 = H, alkyl; R5 = H, alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl; R6 = H, alkyl optionally interrupted by 1-2 N, O, S; R7 = H, alkyl, alkyl interrupted by 1-2 N, O, S, cycloalkyl, aryl, heterocyclyl, aryl, heteroaryl, cyano; R6R7 = atoms to form a 4-7 membered heterocyclic or carbocyclic ring; R8 = H, alkyl, cycloalkyl, cycloalkylalkyl, aralkyl; X = O, S], were prepared as inhibitors of cysteine proteases such as cathepsins B, F, K, L, and S in the treatment of autoimmune diseases, Alzheimer's disease, and atherosclerosis. Thus, (R)-2-cyclohexylmethyl-4-morpholin-4-yl-4-oxobutyric acid (preparation given) in DMF at 0° was treated with EDC, 1-hydroxybenzotriazole, O-benzyl-L-serinamide, and N-methylmorpholine followed by stirring overnight to give N-(2-benzyloxy-1-carbamoylethyl)-2-cyclohexylmethyl-4-morpholin-4-yloxobutyramide. The latter was stirred 1 h with cyanuric chloride in DMF at 0° to give title compound (II). I inhibited cathepsin S with IC50s 100 μM.
IT 324795-10-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of succinic acid diamides as inhibitors of cysteine proteases
(cathepsins) in the treatment of autoimmune diseases, Alzheimer's disease, and atherosclerosis)
RN 324795-10-0 CAPLUS
CN Cyclohexanecarboxamide, N-[(1R)-1-cyano-2-(phenylmethoxy)ethyl]-2-(4-morpholinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L11 ANSWER 44 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

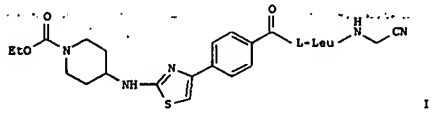
Karen Cheng

L11 ANSWER 41 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:693319 CAPLUS
DOCUMENT NUMBER: 135:257468
TITLE: Preparation of N-(4-thiazolylbenzoyl)-N-(cyanomethyl)-L-leucinamides and analogs as protease inhibitors
INVENTOR(S): Palmer, James T.; Setti, Eduardo L.; Tian, Zong-Qiang; Venkatraman, Shankar; Wang, Dan-Xiong
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068645	A2	20010920	WO 2001-US8332	20010314
WO 2001068645	A3	20020307		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-189694P P 20000315
GI



I

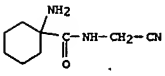
AB The title compds. and their pharmaceutically acceptable salts, N-oxides, prodrugs, protected derivs., or isomers thereof were prepared as cysteine protease inhibitors. For example, stirring a solution of 4-[2-(1-tert-butoxycarbonylpiperidin-4-ylamino)thiazol-4-yl]benzoic acid (preparation given) and the MeSO3H salt of 2S-amino-N-cyanomethyl-4-methylpentanamide overnight at room temperature with PyBOP and diisopropylethylamine in DMF, followed by conversion to the Et ester, yielded I (77%). Test compds. inhibited cathepsin B, K, L, and S (no data). The invention compds. and compns. with a bisphosphonic acid and/or an estrogen receptor agonist are claimed for treating osteoporosis in post-menopausal women (no data).

IT 294622-49-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of N-thiazolylbenzoyl-N-cyanomethyl-L-leucinamides and analogs as cysteine protease inhibitors for treatment of osteoporosis)

RN 294622-49-4 CAPLUS
CN Cyclohexanecarboxamide, 1-amino-N-(cyanomethyl)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 225122-32-7
CMF C9 H15 N3 O

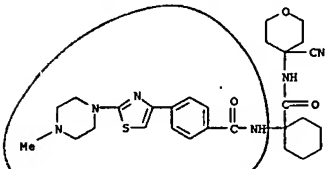


CM 2

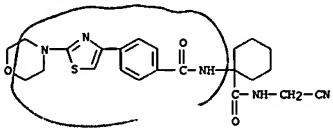
CRN 75-75-2
CMF C H4 O3 S

IT 294622-80-3P 294622-81-4P 294622-98-3P 294622-99-4P 294623-09-9P 294623-10-2P 294623-30-6P 294623-33-9P 294623-35-1P 294623-36-2P 294623-49-7P 361519-34-8P 361519-47-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-thiazolylbenzoyl-N-cyanomethyl-L-leucinamides and analogs as cysteine protease inhibitors for treatment of osteoporosis)

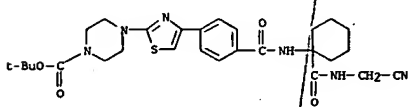
RN 294622-80-3 CAPLUS
CN Benzamide, N-[1-[[(4-cyanotetrahydro-2H-pyran-4-yl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



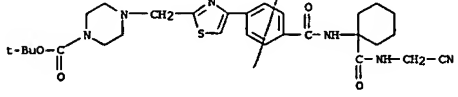
RN 294622-81-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



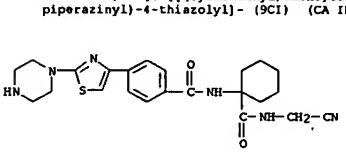
RN 294622-98-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



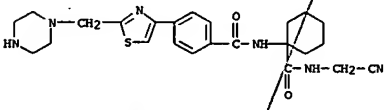
RN 294622-99-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



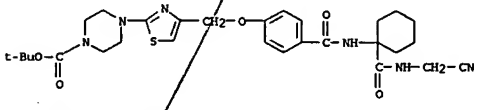
RN 294623-09-9 CAPLUS



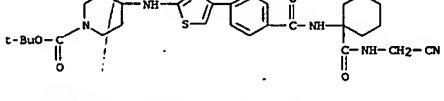
RN 294623-10-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(1-piperazinylmethyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 294623-30-6 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenoxy]methyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



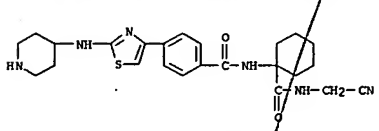
RN 294623-33-9 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



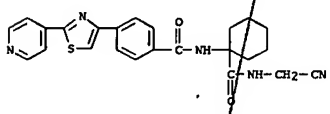
RN 294623-35-1 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-

Karen Cheng

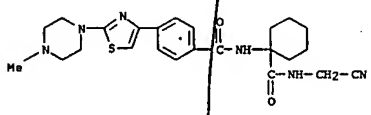
L11 ANSWER 41 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
piperidinylamino)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 294623-36-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-pyridinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 294623-49-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

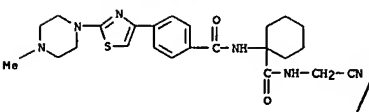


RN 361519-34-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 294623-49-7
CMF C24 H30 N6 O2 S

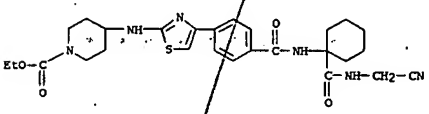
L11 ANSWER 41 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



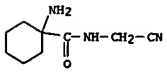
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 361519-47-3 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)



IT 225122-32-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of N-thiazolylbenzoyl-N-cyanomethyl-L-leucinamides and analogs as cysteine protease inhibitors for treatment of osteoporosis)
RN 225122-32-7 CAPLUS
CN Cyclohexanecarboxamide, 1-amino-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



L11 ANSWER 41 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

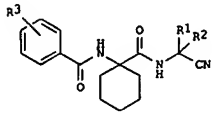
L11 ANSWER 42 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2001:597973 CAPLUS
DOCUMENT NUMBER:	135:180786
TITLE:	Preparation of dipeptide cathepsin K inhibitors
INVENTOR(S):	Missbach, Martin
PATENT ASSIGNEE(S):	Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft Mbh
SOURCE:	PCT Int. Appl., 36 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058886	A1	20010816	WO 2001-EP1359	20010208
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
TW 258473	B	20060721	TW 2001-90102220	20010202
US 2001016207	A1	20010823	US 2001-778302	20010207
US 6642239	B2	20031104		
CA 2396158	A1	20010816	CA 2001-2396158	20010208
TR 200201752	T2	20021021	TR 2002-1752	20010208
EP 1254124	A1	20021106	EP 2001-919270	20010208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001008118	A	20030225	BR 2001-8118	20010208
HU 200300148	A2	20030528	HU 2003-148	20010208
JP 2003522764	T	20030729	JP 2001-558437	20010208
AU 764334	B2	20030814	AU 2001-46426	20010208
NZ 519940	A	20040227	NZ 2001-519940	20010208
CN 1636980	A	20050713	CN 2004-10090944	20010208
RU 2265601	C2	20051210	RU 2002-123350	20010208
RU 2293732	C2	20070220	RU 2005-108133	20010208
ZA 2002006218	A	20030805	ZA 2002-6218	20020805
NO 2002003780	A	20020809	NO 2002-3780	20020809
MX 2002PA07768	A	20021011	MX 2002-PA7768	20020809
HK 1050197	A1	20050513	HK 2003-102397	20030403
US 2003203919	A1	20031030	US 2003-410377	20030409
US 2005267129	A1	20051201	US 2005-195747	20050803
PRIORITY APPLN. INFO.:			GB 2000-3111	A 20000210
			US 2001-778302	A1 20010207
			RU 2001-123350	A 20010208
			WO 2001-EP1359	W 20010208
			US 2003-410377	A1 20030409

OTHER SOURCE(S): MARPAT 135:180786
GI

L11 ANSWER 42 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

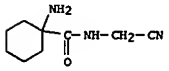


I

AB The title N-[1-(cyanomethylcarbamoyl)cyclohexyl]-4-heterocyclylbenzamides (I) [wherein R1 and R2 = independently H or alkyl, or R1 and R2 together with the C to which they are attached form a cycloalkyl ring; R3 = (un)substituted N-containing heterocycle, especially (cyclo)alkyl-, alkoxyalkyl-, or arylalkyl-substituted piperidinyl or piperazinyl; and pharmaceutically acceptable salts or esters thereof] were prepared as cathepsin K inhibitors. For example, 1-aminocyclohexanecarboxylic acid cyanomethylamide was coupled with 4-[4-(9-fluorenylmethoxycarbonyl)piperazin-1-yl]benzoic acid (3-step preparation given) using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide. bul.HCl in DMF and the piperazine deprotected using piperidine in DMF to afford I [wherein R1 and R2 = H; R3 = piperazinyl]. Although no data for individual compds. is given, I are reported to have Ki values for human cathepsin K of < 50 nM and absolute oral bioavailabilities of 50% to 80%. I are useful for therapeutic or prophylactic treatment of diseases or medical conditions in which cathepsin K is implicated, e.g. inflammation, osteoporosis, rheumatoid arthritis, and osteoarthritis (no data).

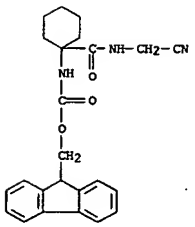
IT 225122-32-7P 354813-09-5P 354813-13-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of N-cyanomethylcarbamoylcyclohexyl heterocyclylbenzamide cathepsin K inhibitors by coupling substituted cyclohexylamines with heterocycylbenzoic acids)

RN 225122-32-7 CAPLUS
CN Cyclohexanecarboxamide, 1-amino-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



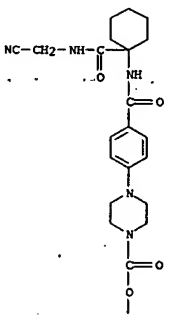
RN 354813-09-5 CAPLUS
CN Carbamic acid, [1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 42 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



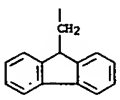
RN 354813-13-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



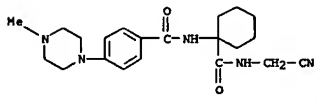
L11 ANSWER 42 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

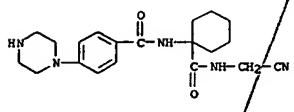


IT 294622-35-8P 354813-10-8P 354813-16-4P
354813-19-7P 354813-22-2P 354813-25-5P
354813-28-8P 354813-31-3P 354813-34-6P
354813-39-1P 354813-43-7P 354813-47-1P
354813-50-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-cyanomethylcarbamoylcyclohexyl heterocyclylbenzamide cathepsin K inhibitors by coupling substituted cyclohexylamines with heterocycylbenzoic acids)

RN 294622-35-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

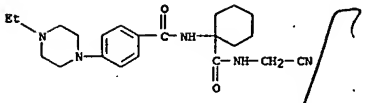


RN 354813-10-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)

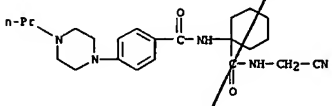


RN 354813-16-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-ethyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

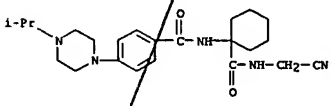
L11 ANSWER 42 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



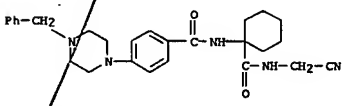
RN 354813-19-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propyl-1-piperazinyl)- (CA INDEX NAME)



RN 354813-22-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[4-(1-methylethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

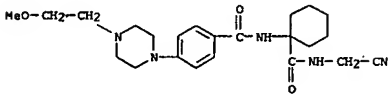


RN 354813-25-5 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[4-(phenylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

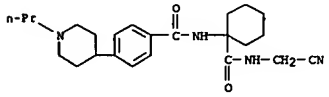


RN 354813-28-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[4-(2-methoxyethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

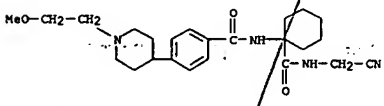
L11 ANSWER 42 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



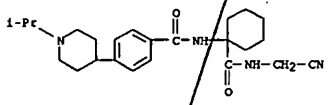
RN 354813-31-3 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-propyl-4-piperidinyl)- (9CI) (CA INDEX NAME)



RN 354813-34-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[1-(2-methoxyethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

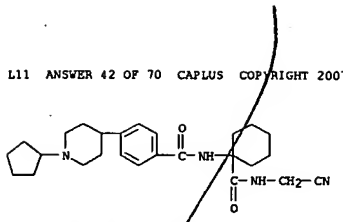


RN 354813-39-1 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

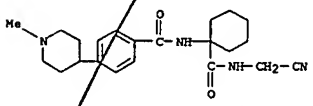


RN 354813-43-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-cyclopentyl-4-piperidinyl)- (9CI) (CA INDEX NAME)

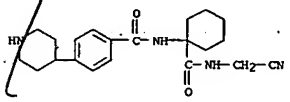
L11 ANSWER 42 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 354813-47-1 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1-methyl-4-piperidinyl)- (9CI) (CA INDEX NAME)



RN 354813-50-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 43 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:208265 CAPLUS
DOCUMENT NUMBER: 134:252348
TITLE: Novel spiroheterocyclic compounds [morpholine-4-carboxylic acid amides of heterocyclic cyclohexylalanine and neopentylglycine derivatives and their analogs], useful as reversible inhibitors of cysteine proteases such as cathepsin S
INVENTOR(S): Emmanuel, Michel J.; Frye, Leah L.; Hickey, Eugene R.; Liu, Weimin; Morwick, Tina M.; Spero, Denice M.; Sun, Sanxing; Thomson, David S.; Ward, Yancey D.; Young, Erick R. R.
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 361 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019816	A1	20010322	WO 2000-US23584	20000828
W: AE, AU, BG, BR, BY, CA, CN, CZ, EE, HR, HU, ID, IL, IN, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, VN, YU, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2385130	A1	20010322	CA 2000-2385130	20000828
AU 200070818	A	20010417	AU 2000-70818	20000828
AU 782246	B2	20050714		
EP 1218372	A1	20020703	EP 2000-959506	20000828
EP 1218372	B1	20030702		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
AT 244235	T	20030715	AT 2000-959506	20000828
JP 2003529546	T	20031007	JP 2001-523393	20000828
PT 1218372	T	20031128	PT 2000-959506	20000828
EE 200200132	A	20031215	EE 2002-132	20000828
ES 2199856	T3	20040301	ES 2000-959506	20000828
HU 200302380	A2	20040301	HU 2003-2380	20000828
BR 2000013966	A	20040615	BR 2000-13966	20000828
NZ 518255	A	20041126	NZ 2000-518255	20000828
RU 2255937	C2	20050710	RU 2002-107433	20000828
TW 230159	B	20050401	TW 2000-89118587	20000911
US 2002058809	A1	20020516	US 2001-1134	20011102
US 6756372	B2	20040629		
BG 106483	A	20021031	BG 2002-106483	20020305
ZA 2002001987	A	20040416	ZA 2002-1987	20020311
NO 2002001207	A	20020312	NO 2002-1207	20020312
NO 323354	B1	20070410		
HR 2002000221	B1	20070131	HR 2002-221	20020312
US 2003225271	A1	20031204	US 2003-422471	20030424
US 7056915	B2	20060606		
US 2003225270	A1	20031204	US 2003-422473	20030424
US 6982272	B2	20060103		
US 2005032792	A1	20050210	US 2004-937533	20040909
US 2005032772	A1	20050210	US 2004-937636	20040909
PRIORITY APPLN. INFO.:			US 1999-153738P P	19990913
			US 2000-222900P P	20000803

L11 ANSWER 43 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

	WO 2000-US23584	W 20000828
	US 2000-655351	A3 20000908
	US 2001-1134	A3 20011102
	US 2003-422471	A1 20030424

OTHER SOURCE(S): MARPAT 134:252348
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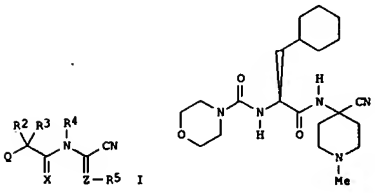

AB Compds. of formula I are claimed [wherein; Q is R1C(=Y)NR4- or R1C(=NR6)NR4- or R1YNR4- or R1C(NR6R8)=N-, where R1 is (cyclo)alkyl(sulfonyl), alkoxy, aryl(sulfonyl) or hetero(aryl)(cyclyl); R2 is H or alkyl; R3 is H, (un)substituted (cyclo)alkyl, alkylene or aryl(alkyl); or R2R3 may form nonarom. carbo- or heterocyclic ring; R4 is H, OH, or alkyl; R5 is bond, H, alkyl optionally interrupted by 1 or 2 O, S, Ph, naphthyl, heterocyclyl, etc.; R6 is H, OH, CN, etc.; R8 is alkyl optionally interrupted by N, O, S, etc.; X, Y are O or S; Z is a spirocyclic junction to certain 4-7 membered ring (substituted)(bridged)(fused)heterocycles]. The compds. are novel, reversible inhibitors of cathepsins S, K, F, L and B, and are useful for treating a variety of autoimmune diseases. Also disclosed are processes for preparing I. Over 100 examples, primarily derived from L-cyclohexylalanine and L-neopentylglycine, are given. Claims cover the same compds. with unspecified stereochem. For example, L-β-cyclohexylalanine Me ester hydrochloride was neutralized, amidated with 4-morpholinecarbonyl chloride, and saponified with LiOH in aqueous MeOH-THF to give N-(4-morpholinecarbonyl)-L-cyclohexylalanine. This acid derivative was coupled with crude 4-amino-4-cyano-1-methylpiperidine using EDC in the presence of HOBT and N-methylmorpholine in DMF, yielding title compound II. Compds. I inhibited human recombinant cathepsin S in vitro with IC50 values of 100 μM or below.

IT 331280-90-1P, [1-(1-Benzyl-3-cyanopyrrolidin-3-ylcarbamoyl)cyclohexyl]carbamic acid tert-butyl ester 331280-92-3P, [1-(1-Benzyl-3-cyanopyrrolidin-3-ylcarbamoyl)cyclohexyl]carbamic acid benzyl ester
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of spiroheterocyclic morpholine derivs. of cyclohexylalanine and neopentylglycine as reversible inhibitors of

L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:666701 CAPLUS
DOCUMENT NUMBER: 133:252050
TITLE: Preparation of novel N-cyanomethyl amide compounds and compositions as protease inhibitors to treat osteoporosis
INVENTOR(S): Bryant, Clifford M.; Palmer, James T.; Rydzewski, Robert M.; Setti, Eduardo L.; Tian, Zong-Qiang; Venkatraman, Shankar; Wang, Dan-Xiong
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055126	A2	20000921	WO 2000-US6837	20000315
WO 2000055126	A3	20010222		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
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CA 2368148	A1	20000921	CA 2000-2368148	20000315
EP 1161415	A2	20011212	EP 2000-916375	20000315
EP 1161415	B1	20050713		
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BR 2000009043	A	20020108	BR 2000-9043	20000315
TR 200103337	T2	20020321	TR 2001-3337	20000315
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HU 200200347	A2	20020629	HU 2002-347	20000315
HU 200200503	A2	20020629	HU 2002-503	20000315
US 6455502	B1	20020924	US 2000-526090	20000315
TR 200201874	T2	20021021	TR 2002-1874	20000315
US 6476026	B1	20021105	US 2000-526485	20000315
JP 2002539192	T	20021119	JP 2000-605557	20000315
EE 200100487	A	20030217	EE 2001-487	20000315
AU 769736	B2	20040205	AU 2000-37486	20000315
PT 1178958	T	20040730	PT 2000-916343	20000315
EP 1452522	A2	20040901	EP 2004-75486	20000315
EP 1452522	A3	20050209		
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ES 2215626	T3	20041016	ES 2000-916343	20000315
AT 299493	T	20050715	AT 2000-916375	20000315
ES 2245303	T3	20060101	ES 2000-916375	20000315
ZA 2001007494	A	20020911	ZA 2001-7494	20010911
ZA 2001007495	A	20020911	ZA 2001-7495	20010911
MX 2001PA09255	A	20020108	MX 2001-PA9255	20010913

L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

NO 2001004484	A	20011026	NO 2001-4484	20010914
BG 106013	A	20020531	BG 2001-106013	20011012
HR 2001000737	A1	20021031	HR 2001-737	20011012
US 2002086996	A1	20020704	US 2001-17851	20011214
US 6593327	B2	20030715		
US 2003096796	A1	20030522	US 2002-205600	20020724
US 2003119788	A1	20030626	US 2002-241001	20020909
US 2004147745	A1	20040729	US 2004-758893	20040115
US 2007015755	A1	20070118	US 2006-533582	20060920

PRIORITY APPLN. INFO.: US 1999-124420P P 19990315
EP 2000-916343 A3 20000315
US 2000-526090 A1 20000315
US 2000-526485 A3 20000315
WO 2000-US6837 W 20000315
US 2002-205600 B1 20020724
US 2004-758893 B1 20040115

OTHER SOURCE(S): MARPAT 133:252050

AB Title compds. [R1R2NCR3R4CN; R1 = R11R7NCR5R9X1, R11R8NCR6R10X2NR7CR5R9CX1; X1, X2 independently = CO, CH2SO2; R5, R6 independently = H, C1-6alkyl; R7, R8 independently = H, C1-6alkyl; R9, R10 independently = (un)substituted-C1-6alkyl; R9-R7 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R10-R8 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R5-R9 = C3-8cycloalkylene, C3-8heterocycloalkylene; R10-R6 = C3-8cycloalkylene, C3-8heterocycloalkylene; R11 = X4X5R18; X4 = CO, COCO, SO2; X5 = bond, O, NH; R18 = C1-6alkyl; R2 = H, C1-6alkyl; R3 = H, C1-6alkyl; R4 = CN, COOH, COOC1-6alkyl; R2-R4 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R4-R3 = C3-8cycloalkylene, C3-8heterocycloalkylene], N-oxide, prodrug, isomers, pharmaceutically acceptable salts, and composition are prepared as therapeutically effective estrogen receptor agonist. Title compds. are claimed in treating osteoporosis in post-menopausal woman in which cathepsin K activity contributes to the pathol. and symptomatol. of the disease. Thus, the title compound (S)-C6H5CH2OCONHCH(CH2CH(CH3)2)CONHCH2CN was prepared

IT 225122-33-8P 294622-31-4P 294622-33-6P
294622-34-7P 294622-35-8P 294622-36-9P
294622-37-0P 294622-39-2P 294622-41-6P
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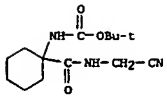
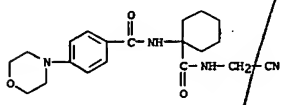
294624-11-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel N-cyanomethyl amides and compns. as protease inhibitors)

RN 225122-33-8 CAPLUS
CN Carbamic acid, [1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

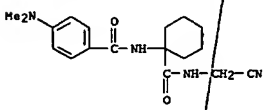
L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



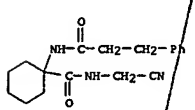
RN 294622-31-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 294622-33-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

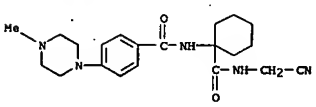


RN 294622-34-7 CAPLUS
CN Benzenepropanamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

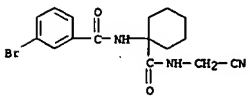


RN 294622-35-8 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

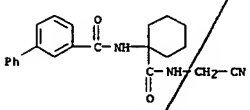
L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 294622-36-9 CAPLUS
CN Benzamide, 3-bromo-N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)



RN 294622-37-0 CAPLUS
CN [1,1'-Biphenyl]-3-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)



RN 294622-39-2 CAPLUS
CN Benzamide, N-[1-[[(1-cyanocyclopropyl)amino]carbonyl]cyclohexyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

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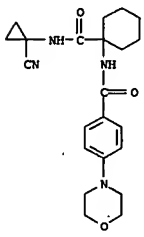
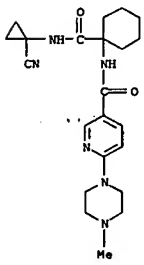
L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

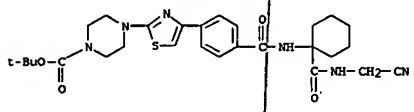


RN 294622-41-6 CAPLUS
CN 3-Pyridinecarboxamide, N-[1-[[[(1-cyanocyclopropyl)amino]carbonyl]cyclohexyl]-6-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

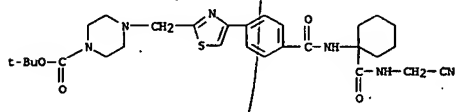


RN 294622-42-7 CAPLUS
CN Carbamic acid, [1-[[[(1-cyanocyclopropyl)amino]carbonyl]cyclohexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

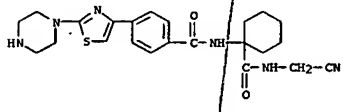
L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



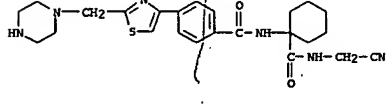
RN 294622-99-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 294623-09-9 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(1-piperazinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

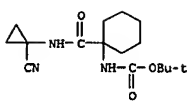


RN 294623-10-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(1-piperazinylmethyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

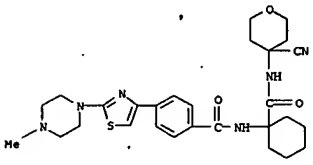


RN 294623-30-6 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenoxy]methyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

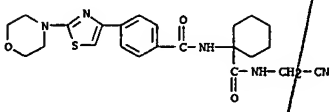
L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 294622-80-3 CAPLUS
CN Benzamide, N-[1-[[(4-cyanotetrahydro-2H-pyran-4-yl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

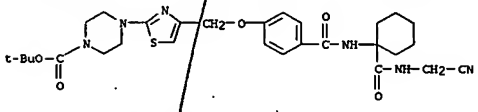


RN 294622-81-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-morpholinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)

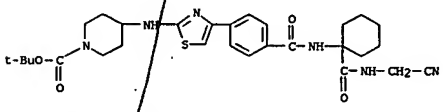


RN 294622-98-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

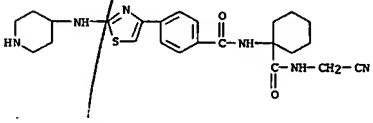
L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



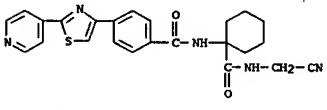
RN 294623-33-9 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[4-[4-[[[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]amino]carbonyl]phenyl]-2-thiazolyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 294623-35-1 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-piperidinylamino)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 294623-36-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-pyridinyl)-4-thiazolyl]- (9CI) (CA INDEX NAME)



RN 294623-49-7 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

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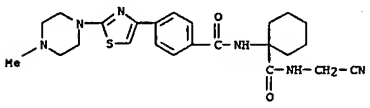
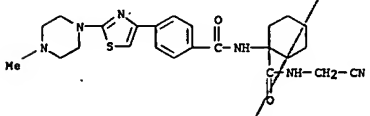
L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 294624-11-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 294623-49-7
CMF C24 H30 N6 O2 S



CM 2.

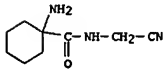
CRN 76-05-1
CMF C2 H F3 O2

IT 294622-49-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel N-cyanomethyl amides and compns. as protease inhibitors)
RN 294622-49-4 CAPLUS
CN Cyclohexanecarboxamide, 1-amino-N-(cyanomethyl)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 225122-32-7

L11 ANSWER 45 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CMF C9 H15 N3 O



CM 2

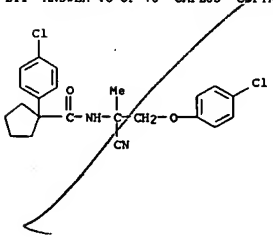
CRN 75-75-2
CMF C H4 O3 S

L11 ANSWER 46 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:708444 CAPLUS
DOCUMENT NUMBER: 131:310455
TITLE: Preparation of acylaminoacetonitriles as agricultural and horticultural insecticides
INVENTOR(S): Andoh, Nobuharu; Sanpei, Osamu; Sakata, Kazuyuki
PATENT ASSIGNEE(S): Nihon Nohyaku Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 63 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 953565	A2	19991103	EP 1999-107461	19990428
EP 953565	A3	20021204		
EP 953565	B1	20040908		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6239077	B1	20010529	US 1999-295319	19990421
TW 585849	B	20040501	TW 1999-88106732	19990427
EP 1445251	A1	20040811	EP 2004-10346	19990428
EP 1445251	B1	20061227		
R: CH, DE, FR, GB, IT, LI				
CN 1234177	A	19991110	CN 1999-105289	19990430
CN 1132516	B	20031231		
AU 9926027	A	19991111	AU 1999-26027	19990430
AU 752112	B2	20020905		
JP 2000026392	A	20000125	JP 1999-124560	19990430
PRIORITY APPLN. INFO.:			JP 1998-137806	A 19980501
			EP 1999-107461	A3 19990428

OTHER SOURCE(S): MARPAT 131:310455
AB Ar1QdCONR3C(CN)R4(CR5R6)aW(CR7R8)bAr2 [I; Ar1, Ar2 = (substituted) Ph, PhO, pyridyl, pyridyloxy, naphthyl; Q = CR1R2; R1, R2 = H, halo, (halo)alkyl, (halo)alkoxy, (substituted) cycloalkyl; R1R2 = (substituted) C2-6 alkylene, CH:CH, C.tplbond.C; d = 0, 1; R3 = H, (halo)alkyl; R4-R8 = H, halo, (halo)alkyl; W = O, S, SO2, NR9; R9 = H, alkyl; a, b = 0-4], were prepared Thus, 4-chlorophenol, bromoacetaldehyde di-Me acetal, K2CO3, and cat. NaI were refluxed 3 h in DMF to give 4-chlorophenoxyacetaldehyde di-Me acetal. This was refluxed with aqueous HCl in acetone to give crude 4-chlorophenoxyacetaldehyde, which was stirred with NaCN and NH4Cl in aqueous
NH3 to give a reside. This was stirred with 4-chlorophenylacetyl chloride and Et3N in THF to give I (Ar1, Ar2 = 4-ClC6H4; R1-R8 = H; W = O; a, d = 1; b = 0). Numerous I at 500 ppm gave 100% kill of Plutella xylostella on cabbage seedlings.
IT 247198-01-2P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of acylaminoacetonitriles as agricultural and horticultural insecticides)
RN 247198-01-2 CAPLUS
CN Cyclopentanecarboxamide, N-[2-(4-chlorophenoxy)-1-cyano-1-methylethyl]-1-(4-chlorophenyl)- (9CI) (CA INDEX NAME)

L11 ANSWER 46 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



Karen Cheng

L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:325961 CAPLUS
DOCUMENT NUMBER: 130:352553
TITLE: Synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins
INVENTOR(S): Altmann, Eva; Betschart, Claudia; Gohda, Keigo; Horiuchi, Miyuki; Lattmann, Rene; Missbach, Martin; Sakaki, Junichi; Takai, Michihiro; Teno, Naoki; Cowen, Scott Douglas; Greenspan, Paul David; McQuire, Leslie Wighton; Tommasi, Ruben Alberto; Van Duzer, John Henry
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft mbH
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924460	A2	19990520	WO 1998-EP6937	19981103
WO 9924460	A3	19990902		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306313	A1	19990520	CA 1998-2306313	19981103
AU 9914873	A	19990531	AU 1999-14873	19981103
AU 751669	B2	20020822		
EP 1028942	A2	20000823	EP 1998-958887	19981103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9813197	A	20000829	BR 1998-13197	19981103
TR 200001189	T2	20000921	TR 2000-200001189	19981103
JP 2001522862	T	20011120	JP 2000-520468	19981103
HU 200004400	A2	20020429	HU 2000-4400	19981103
RU 2201420	C2	20030327	RU 2000-114821	19981103
ZA 9810073	A	19990505	ZA 1998-10073	19981104
TW 527362	B	20030411	TW 1998-87118553	19981105
NO 2000002320	A	20000704	NO 2000-2320	20000502
MX 2000PA04375	A	20001211	MX 2000-PA4375	20000504
US 6353017	B1	20020305	US 2000-643639	20000822
US 2004029814	A1	20040212	US 2003-342872	20030115
US 2004110806	A1	20040610	US 2003-694672	20031028
US 2006235220	A1	20061019	US 2006-374995	20060315

PRIORITY APPLN. INFO.:

GB 1997-23407	A	19971105
US 1997-108160P	P	19971205
US 1997-985973	A	19971205
WO 1998-EP6937	W	19981103
US 1998-186223	B1	19981104
US 2000-643639	A1	20000822

L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

US 2002-54590	B1	20020122
US 2003-342872	A1	20030115
US 2003-694672	B1	20031028

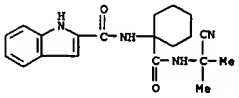
OTHER SOURCE(S): MARPAT 130:352553

AB N-terminal substituted dipeptide nitriles R(L)xX1NHCR2R3C(:Y)NHCR4R5CN [R is optionally substituted aryl, alkyl, alkenyl, alkynyl, heterocyclyl; R2, R3 = H, optionally substituted alkyl, cycloalkyl, bicycloalkyl, or aryl-, biaryl-, cycloalkyl, bicycloalkylalkyl; R2 and R3 together represent alkylene, optionally interrupted by O, S, or NR6, where R6 is H, alkyl, arylalkyl; or R2 or R3 are linked by alkylene to the adjacent nitrogen to form a ring; R4, R5 = H, optionally substituted alkyl, arylalkyl, CO2R7, CONR7R8 (R7 is optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, or heterocyclyl and R8 is H or optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, heterocyclyl), etc.; R4 and R5 together represent alkylene, optionally interrupted by O, S, or NR6; X1 = CO, CS, SO, SO2, P(O)OR6; Y = O, S; L is optionally substituted Het, Het-CH2, CH2-Het (Het = O, N, or S); x = zero or 1] were prepared as inhibitors of cysteine cathepsins, e.g., cathepsins B, K, L and S, and can be used for the treatment of cysteine cathepsin dependent diseases and conditions. Thus, N-[2-[(3-carboxyphenyl)methoxy]-1(S)-cyanoethyl]-3-methyl-Na-(2,2-diphenylacetyl)-L-phenylalaninamide was prepared and shown to have IC50 = 5 nM for inhibition of cathepsin B.

IT 225118-47-8P 225118-54-7P 225118-55-8P
225118-56-9P 225118-57-0P 225118-58-1P
225118-59-2P 225118-60-5P 225118-61-6P
225118-62-7P 225118-63-8P 225118-64-9P
225118-65-0P 225118-66-1P 225118-67-2P
225118-68-3P 225118-69-4P 225118-70-7P
225118-71-8P 225118-72-9P 225118-73-0P
225118-74-1P 225118-75-2P 225118-76-3P
225118-77-4P 225118-78-5P 225118-79-6P
225118-80-9P 225118-81-0P

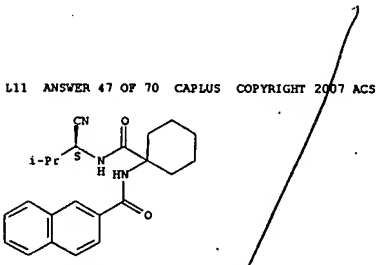
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins)

RN 225118-47-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[[(1-cyano-1-methylethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

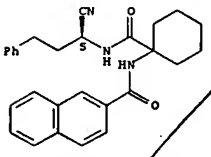


RN 225118-54-7 CAPLUS
CN 2-Naphthalenecarboxamide, N-[1-[[[(1S)-1-cyano-3-phenylpropyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

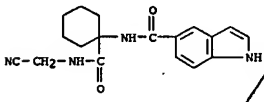
Absolute stereochemistry.



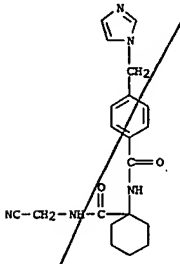
L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 225118-55-8 CAPLUS
CN 1H-Indole-5-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)



RN 225118-56-9 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1H-imidazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



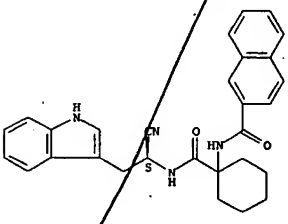
RN 225118-57-0 CAPLUS
CN 2-Naphthalenecarboxamide, N-[1-[[[(1S)-1-cyano-2-methylpropyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

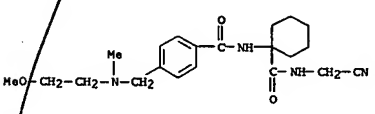
L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 225118-58-1 CAPLUS
CN 2-Naphthalenecarboxamide, N-[1-[[[(1S)-1-cyano-2-(1H-indol-3-yl)ethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 225118-59-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-[[(2-methoxyethyl)methylamino]methyl]- (9CI) (CA INDEX NAME)



RN 225118-60-5 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-3-(1H-imidazol-1-ylmethyl)- (9CI) (CA INDEX NAME)

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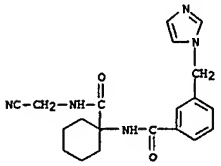
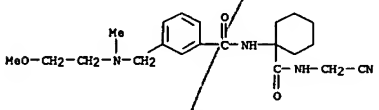
L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

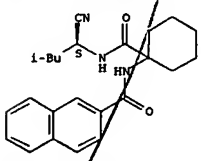


RN 225118-61-6 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-3-[[(2-methoxyethyl)methylamino]methyl]- (9CI) (CA INDEX NAME)



RN 225118-62-7 CAPLUS
CN 2-Naphthalenecarboxamide, N-[1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

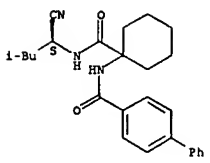
Absolute stereochemistry.



RN 225118-63-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

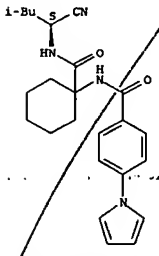
Absolute stereochemistry.

L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 225118-64-9 CAPLUS
CN Benzamide, N-[1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-4-(1H-pyrrol-1-yl)- (9CI) (CA INDEX NAME)

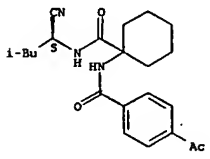
Absolute stereochemistry.



RN 225118-65-0 CAPLUS
CN Benzamide, 4-acetyl-N-[1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

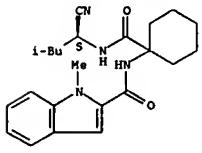
Absolute stereochemistry.

L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

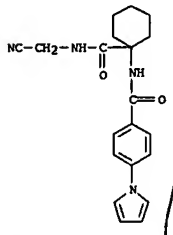


RN 225118-66-1 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

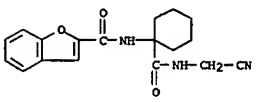


RN 225118-67-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1H-pyrrol-1-yl)- (9CI) (CA INDEX NAME)



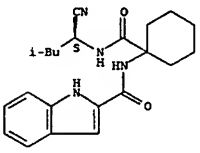
RN 225118-68-3 CAPLUS
CN 2-Benzofurancarboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

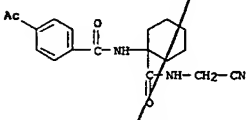


RN 225118-69-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

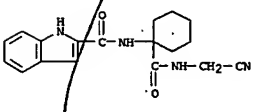
Absolute stereochemistry.



RN 225118-70-7 CAPLUS
CN Benzamide, 4-acetyl-N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

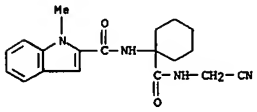


RN 225118-71-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

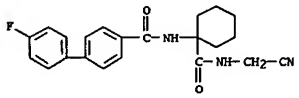


RN 225118-72-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

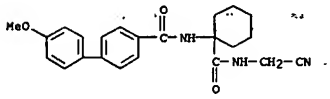
L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



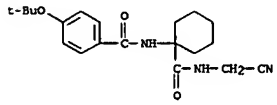
RN 225118-73-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4'-fluoro- (9CI) (CA INDEX NAME)



RN 225118-74-1 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4'-methoxy- (9CI) (CA INDEX NAME)



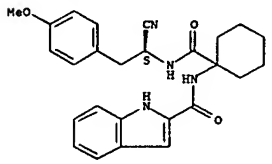
RN 225118-75-2 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(1,1-dimethylethoxy)- (9CI) (CA INDEX NAME)



RN 225118-76-3 CAPLUS

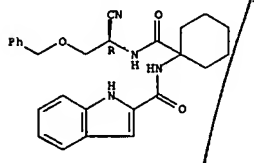
L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 1H-Indole-2-carboxamide, N-[1-[[[(1S)-1-cyano-2-(4-methoxyphenyl)ethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



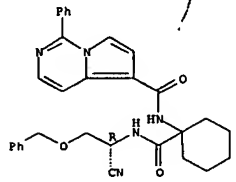
RN 225118-80-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 225118-81-0 CAPLUS
CN Pyrrolo[1,2-c]pyrimidine-5-carboxamide, N-[1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl]-1-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 225122-32-7

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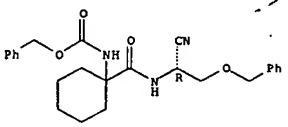
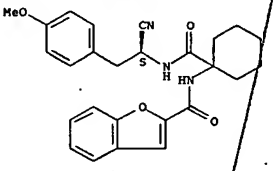
L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Carbamic acid, [1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



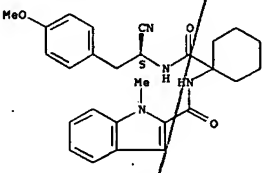
RN 225118-77-4 CAPLUS
CN 2-Benzofurancarboxamide, N-[1-[[[(1S)-1-cyano-2-(4-methoxyphenyl)ethyl]amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



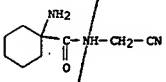
RN 225118-78-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[[[(1S)-1-cyano-2-(4-methoxyphenyl)ethyl]amino]carbonyl]cyclohexyl]-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

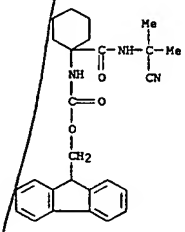


RN 225118-79-6 CAPLUS

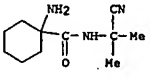
L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins)
RN 225122-32-7 CAPLUS
CN Cyclohexanecarboxamide, 1-amino-N-(cyanomethyl)- (9CI) (CA INDEX NAME)



IT 225122-24-7P 225122-25-8P 225122-33-8P
225122-34-9P 225122-35-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins)
RN 225122-24-7 CAPLUS
CN Carbamic acid, [1-[[(1-cyano-1-methylethyl)amino]carbonyl]cyclohexyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

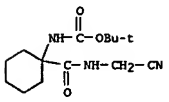


RN 225122-25-8 CAPLUS
CN Cyclohexanecarboxamide, 1-amino-N-(1-cyano-1-methylethyl)- (9CI) (CA INDEX NAME)

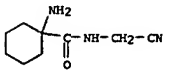


RN 225122-33-8 CAPLUS
CN Carbamic acid, [1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L11 ANSWER 47 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

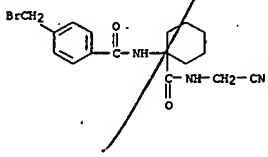


RN 225122-34-9 CAPLUS
CN Cyclohexanecarboxamide, 1-amino-N-(cyanomethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 225122-35-0 CAPLUS
CN Benzamide, 4-(bromomethyl)-N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]- (9CI) (CA INDEX NAME)



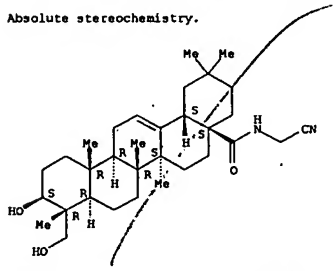
L11 ANSWER 48 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

nephritis, are prepd. Thus, N-(2-methoxyethyl)-3β,23(4α)-dihydroxyolean-12-en-28-amide (II) reacted with p-methoxybenzyloxyacetic acid in CH2Cl2 contg. 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide HCl and 4-dimethylaminopyridine to give the title compd. N-(2-methoxyethyl)-3β-hydroxy-23(4α)-[(4-methoxybenzyloxy)acetoxy]olean-12-en-28-amide. N-(2-methoxyethyl)-3β-hydroxy-23(4α)-hydroxyacetoxyolean-12-en-28-amide (also prepd.) at 1 mg/Kg p.o. effected higher inhibition of mesangium cells in rats with nephritis induced by Thy-1 antiserum than II at 30 mg/Kg p.o. Pharmaceutical compns. contg. I are described.

IT 219550-64-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of triterpene derivs. for treatment of nephritis)

RN 219550-64-8 CAPLUS
CN Olean-12-en-28-amide, N-(cyanomethyl)-3,23-dihydroxy-, (3β,4α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



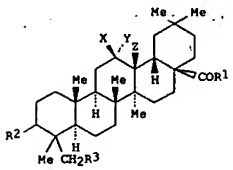
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 48 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:27844 CAPLUS
DOCUMENT NUMBER: 130:95698
TITLE: Triterpene derivatives and medicinal composition
INVENTOR(S): Segawa, Jun; Matsuoka, Masato; Yoshifusa, Hiroto; Nakamura, Akio
PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9858946	A1	19981230	WO 1998-JP2779	19980619
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9880382	A	19990104	AU 1998-80382	19980619
PRIORITY APPLN. INFO.:			JP 1997-167484	A 19970624
			WO 1998-JP2779	W 19980619

OTHER SOURCE(S): MARPAT 130:95698
GI



I

AB Oleanane derivs. I [X, Y, and Z are any of the combinations (1) to (4): (1) X and Z in combination represent a bond, and Y = H, (2) X and Y in combination represent oxo, and Z = H, (3) X = OH, and Y and Z each = H, (4) Y = OH, and X and Z each = H; R1 = OH, optionally substituted monoalkylamino, optionally substituted cyclic amino, optionally substituted alkoxy, etc.; R2 = OH, optionally substituted sulfonyloxy, optionally substituted OP(O)(OH)2, optionally substituted acyloxy, etc.; and R3 = H, OH, optionally substituted sulfonyloxy, optionally substituted OP(O)(OH)2, optionally substituted acyloxy, etc.], useful for treatment of

L11 ANSWER 49 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:87758 CAPLUS
DOCUMENT NUMBER: 128:167714
TITLE: Preparation of substituted 2-aminocycloalkanecarboxylate peptide derivatives as thrombin inhibitors
INVENTOR(S): Di Bugno, Cristina; Giorgi, Raffaello; Harmat, Nicholas
PATENT ASSIGNEE(S): A. Menarini Industrie Farmaceutiche Riunite S.R.L., Italy; Giorgi, Raffaello; Harmat, Nicholas
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803540	A2	19980129	WO 1997-EP3774	19970715
WO 9803540	A3	19980409		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9735437	A	19980210	AU 1997-35437	19970715
PRIORITY APPLN. INFO.:			IT 1996-MI1512	A 19960719
			WO 1997-EP3774	W 19970715

OTHER SOURCE(S): MARPAT 128:167714
GI

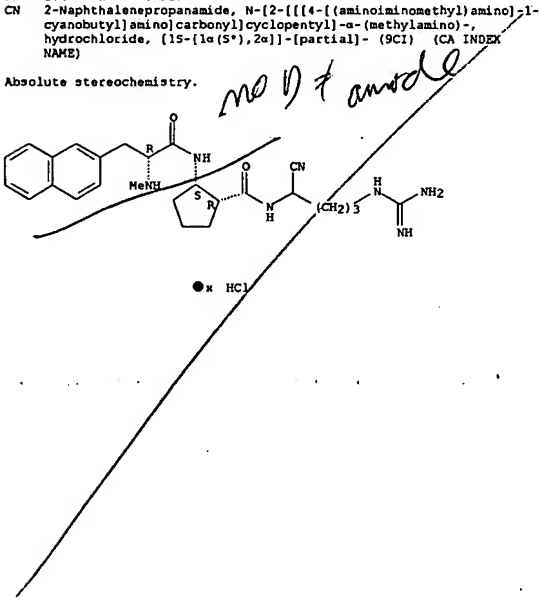
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [A = (CH2)n, CH:CH, n = 1-3; W = CN, CH2OH, COR1, BR2R3; R1 = H, OR4, CONHR4, CH2Cl, CF3, C2F5; R2, R3 = independently OR4, R2R3 = diol residue; R4 = H, C1-7 alkyl, aryl, C7-10 arylalkyl; Y = (un)substituted aryl, (CH2)m-T, CH2C6H4-T, m = 3-6, T = H, OH, C1-3 alkoxy, amino, amidino, imidazole, guanidino, isothioureido; Q = H, C1-7 alkyl; L = (CH2)p, OCH2, SCH2, p = 0-3; Ar = aromatic group; X = H, C1-7 alkyl, MeSO2, tosyl, PhSO2, Me3CO2C (Boc), PhCH2O2C (Cbz), Ac, Bz] with inhibitory activity on serine proteases, processes for the preparation thereof, pharmaceutical compns. containing them and the use thereof as therapeutical agents, are described. Thus, monoester II was converted into amino acid III via treatment with DPPA, saponification, and hydrogenolysis. III underwent sequential coupling with protected methylphenylalanine active ester Z-D-MePhe-OTCP (TCP = 2,4,5-trichlorophenyl) and protected arginine lactam to give protected tripeptide analog IV, which was reduced with LiAlH4 and deprotected to give desired title compound V as its HCl salt. The prepared compds. I were tested as thrombin inhibitors in an in vitro assay, and all compds. showed IC50 values lower than 5 nM.

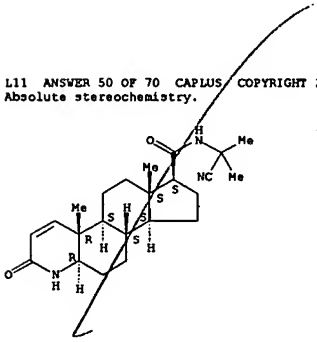
IT 202868-28-8P

L11 ANSWER 49 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted aminoalkanecarboxylate peptide derivs. as thrombin inhibitors)
RN 202868-28-8 CAPLUS
CN 2-Naphthalenepropanamide, N-[2-[[[4-[(aminoiminomethyl)amino]-1-cyanobutyl]amino]carbonyl]cyclopentyl]-α-(methylamino)-, hydrochloride, [1S-[1α(S*),2α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 50 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Absolute stereochemistry.



L11 ANSWER 50 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:617993 CAPLUS
DOCUMENT NUMBER: 127:272793
TITLE: Antiproliferative combinations, containing raf-targeted oligonucleotides and chemotherapeutic compounds
INVENTOR(S): Muller, Marcel; Geiger, Thomas; Altmann, Karl-Heinz; Fabbro, Doriano; Monia, Brett
PATENT ASSIGNEE(S): Novartis AG, Switz.
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732604	A1	19970912	WO 1997-EP875	19970224
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9720925	A	19970922	AU 1997-20925	19970224
ZA 9701936	A	19970908	ZA 1997-1936	19970306
PRIORITY APPLN. INFO.:			US 1996-612787	A 19960307
			WO 1997-EP875	W 19970224

AB The invention relates to combinations of raf-targeted (especially c-raf-targeted) deoxyribo- and ribo-oligonucleotides and derivs. thereof with other chemotherapeutic compds., as well as to pharmaceutical prepns. and/or therapies, in relation to disease states which respond to such oligonucleotides or oligonucleotide derivs., especially to modulation of the activity of a regulatory protein. In particular, the invention relates to products or combinations comprising antisense oligonucleotides or oligonucleotide derivs. targeted to nucleic acids encoding raf and other (preferably standard) chemotherapeutics, either in fixed combination or for chronol. staggered or simultaneous administration, and the combined use of both classes of compds., either in fixed combination or for chronol. staggered or simultaneous administration, for the treatment of proliferative diseases, especially tumor diseases, that can be treated by inhibition of raf activity, i.e., where the antisense oligonucleotides or oligonucleotide derivs. are targeted to nucleic acids encoding the regulatory protein raf or active mutated derivs. thereof.
IT 149281-19-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(raf-targeted oligonucleotide-chemotherapeutic compound antiproliferative combinations)
RN 149281-19-6 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-methylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

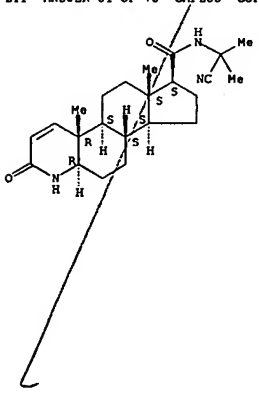
L11 ANSWER 51 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:617979 CAPLUS
DOCUMENT NUMBER: 127:283393
TITLE: Combinations of drugs with antisense oligonucleotides for treatment of proliferative diseases
INVENTOR(S): Muller, Marcel; Geiger, Thomas; Altmann, Karl-Heinz; Fabbro, Doriano; Dean, Nicholas Mark; Monia, Brett; Bennett, Clarence Frank
PATENT ASSIGNEE(S): Novartis A.-G., Switz.
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732589	A1	19970912	WO 1997-EP876	19970224
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5744460	A	19980428	US 1996-612775	19960307
AU 9720926	A	19970922	AU 1997-20926	19970224
ZA 9701937	A	19970908	ZA 1997-1937	19970306
PRIORITY APPLN. INFO.:			US 1996-612775	A 19960307
			WO 1997-EP876	W 19970224

AB The invention relates to combinations of PKC-targeted (especially PKC-α-targeted) deoxyribo- and ribo-oligonucleotides and derivs. thereof with other chemotherapeutic compds., as well as to pharmaceutical prepns. and/or therapies, in relation to disease states which respond to such oligonucleotides or oligonucleotide derivs., especially to modulation of the activity of a regulatory protein. In particular, the invention relates to products or combinations comprising antisense oligonucleotides or oligonucleotide derivs. targeted to nucleic acids encoding human PKC and other (preferably standard) chemotherapeutics, either in fixed combination or for chronol. staggered or simultaneous administration, and the combined use of both classes of compds., either in fixed combination or for chronol. staggered or simultaneous administration, for the treatment of proliferative diseases, especially tumor diseases, that can be treated by inhibition of PKC activity, i.e., where the antisense oligonucleotides or oligonucleotide derivs. are targeted to nucleic acids encoding the regulatory protein PKC or active mutated derivs. thereof.
IT 149281-19-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of drugs with antisense oligonucleotides for treatment of proliferative diseases)
RN 149281-19-6 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-methylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

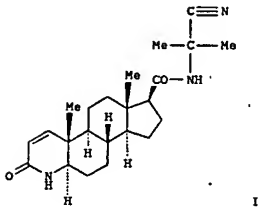
Absolute stereochemistry.

L11 ANSWER 51 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L11 ANSWER 52 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:364294 CAPLUS
DOCUMENT NUMBER: 125:76739
TITLE: CGP 53153: a new potent inhibitor of 5α-reductase
AUTHOR(S): Haeusler, A.; Allegrini, P. R.; Biollaz, M.; Batzl, Ch.; Scheidegger, E.; Bhatnagar, A. S.
CORPORATE SOURCE: Research Department, CIBA-GEIGY Ltd., Basel, CH-4002, Switz.
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1996), 57(3/4), 187-195
CODEN: JSBBEZ; ISSN: 0960-0760
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB CGP 53153 (N-2-(cyano-2-propyl)-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide; I) is a steroidal inhibitor of 5α-reductase, the enzyme which effects the conversion of testosterone (T) to 5α-dihydrotestosterone (DHT). In vitro, I competitively inhibited rat microsomal 5α-reductase from prostate by 50% (IC50) at 36 nM compared to the reference compound finasteride which inhibited 5α-reductase with an IC50 of 11 nM in the same system. In vivo, inhibition of 5α-reductase activity was characterized in three different test systems. Inhibition of 5α-reductase activity was first assessed in a standard test designed to compare directly the potency of different 5α-reductase inhibitors. This test assesses potency through the inhibition of prostate growth in juvenile castrate male rats treated with a standard dose of T-propionate (1 mg/kg, s.c.) and a 5α-reductase inhibitor administered orally at various doses for 4 days. I and finasteride significantly reduced T-propionate-mediated prostate growth by about 25% (ED25) compared to T-propionate-treated controls at oral doses of 0.01 and 0.1 mg/kg, resp. Second, the effects on prostate weight were studied in normal adult male rats treated orally once daily for 14 days with 1, 3 and 10 mg/kg I and with 10 mg/kg finasteride. I significantly reduced prostate weight at 3 and 10 mg/kg by 31% and 37%, resp., compared to vehicle-treated controls, whereas the dose of 10 mg/kg finasteride did not

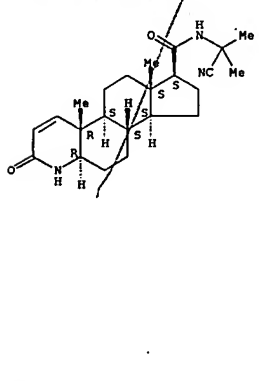
L11 ANSWER 52 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

significantly reduce prostate wt. Third, the effects on prostate vol. were studied in normal 6-9-yr-old male dogs treated orally once daily with 5 mg/kg I and with 5 mg/kg finasteride for 12 wk. Prostate vol. was monitored with magnetic resonance imaging every 2 wk beginning 6 wk before start of the treatment with 5α-reductase inhibitors and ending after a recovery period of 8 wk after termination of treatment. Treatment for 12 wk with both I and finasteride was equally effective in reducing prostate vol. by >70% in individual dogs. Anti-androgenic potency of I and finasteride was assessed in juvenile castrate male rats treated with DHT-propionate (1 mg/kg, s.c.) and a 5α-reductase inhibitor (p.o.) for 4 days. Neither I nor finasteride given at a dose of 10 mg/kg had any significant effect on DHT-propionate-mediated prostate growth, whereas the ref. antiandrogen flutamide given at a dose of 10 mg/kg reduced prostate wt. to levels comparable to those seen in untreated castrate animals. For I, the dose of 10 mg/kg is 1000-fold higher than the ED25 for 5α-reductase inhibition in vivo. In conclusion, both I and finasteride are potent inhibitors of the rat 5α-reductase enzyme system in vitro without showing any antiandrogenic effects in vivo. Both I and finasteride were equally potent in reducing prostate vol. in aged male dogs, whereas in rats, I is up to 10 times more potent than finasteride in reducing prostate wt. as shown in two different rat models.

IT 149281-19-6, CGP 53153
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CGP 53153 inhibition of 5α-reductase and prostate growth)

RN 149281-19-6 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-methylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 53 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1994:244394 CAPLUS
DOCUMENT NUMBER: 120:244394
TITLE: Dibenzo-fused derivatives of bicyclo[2.2.2]octane as cholecystokinin inhibitors
INVENTOR(S): Kalindjian, Sarkis Barret; Low, Caroline Minli Rachel; Mcdonald, Iain Mair; Hull, Robert Antony David; Shankley, Nigel Paul; Buck, Ildiko Maria; Steel, Katherine Isobel Mary; Davies, Jonathan Michael Richar; Dunstone, David John; et al.
PATENT ASSIGNEE(S): James Black Foundation Ltd., UK
SOURCE: PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

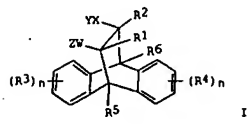
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316982	A1	19930902	WO 1993-GB346	19930219
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9335097	A	19930913	AU 1993-35097	19930219
ZA 9301193	A	19940819	ZA 1993-1193	19930219
EP 626942	A1	19941207	EP 1993-904230	19930219
EP 626942	B1	19970423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07504184	T	19950511	JP 1993-514633	19930219
HU 71499	A2	19951128	HU 1994-2280	19930219
AT 152095	T	19970515	AT 1993-904230	19930219
US 5514683	A	19960507	US 1994-288185	19940809
NO 9403055	A	19941011	NO 1994-3055	19940818
FI 9403817	A	19940819	FI 1994-3817	19940819

PRIORITY APPLN. INFO.:

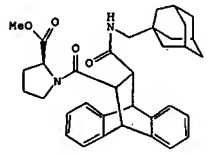
GB 1992-3608	A	19920220
GB 1992-13093	A	19920619
GB 1992-24629	A	19921124
WO 1993-GB346	A	19930219
GB 1993-16722	A	19930812

OTHER SOURCE(S): MARPAT 120:244394
GI

L11 ANSWER 53 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I



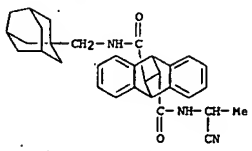
II

AB Title compds. I [W = CO, SO, SO2; X = CO, SO, SO2, COCH2 (with CO end bound to Y), provided that ≥1 of W and X contains CO; Y = certain (un)substituted OH or NH2 groups; Z = different (un)substituted OH or NH2 groups; R1 = H, Me, halo, (amidated or esterified) CO2H or CH2CO2H; R2 = groups for R1, or CO2' (Z' = Z) when Z is absent and W = H; or R1R2 = pi bond; R3, R4 = halo, amino, NO2, cyano, SO2NH2, alkyl, alkoxy, (amidated or esterified) CO2H; R5, R6 = H, R3; m, n = 0-4, provided that both are ≤ 2 unless R3 or R4, resp., are exclusively halo] were prepared as ligands binding at cholecystokinin (CCK) and gastrin receptors. Thus, 2,3,5,6-dibenzobicyclo[2.2.2]octane-7,8-dicarboxylic acid anhydride reacted with 1-adamantanemethylamine, the resultant acid-amide was condensed with H-L-Pro-OCH2Ph.HCl using PyBOP, and the benzyl ester function was hydrogenolyzed and reesterified with diazomethane to give title compound cis-II as a mixture of 2 diastereomers which were separated by repeated crystallization These isomers bound to CCKB receptors (mouse cortical membrane) with pKi = 5.8 and 7.3. Included are 238 synthetic examples, 1H NMR data for all final products (free bases or N-methyl-D-glucamine salts), and receptor-binding results (CCKA, CCKB, and gastrin) for most I.

IT 153459-15-5P 153543-51-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as CCK and gastrin antagonist)

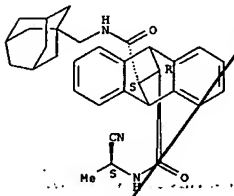
RN 153459-15-5 CAPLUS
CN 9,10-Ethanoanthracene-11,12-dicarboxamide, N-(1-cyanoethyl)-9,10-dihydro-N'-(tricyclo[3.3.1.13,7]dec-1-ylmethyl)-, [11S-[11α(R*),12α]]- (9CI) (CA INDEX NAME)

L11 ANSWER 53 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 153543-51-2 CAPLUS
CN 9,10-Ethanoanthracene-11,12-dicarboxamide, N-(1-cyanoethyl)-9,10-dihydro-N'-(tricyclo[3.3.1.13,7]dec-1-ylmethyl)-, [11R-[11α(S*),12α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



fused

L11 ANSWER 54 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1993:603857 CAPLUS
DOCUMENT NUMBER: 119:203857
TITLE: Preparation of modified peptides transportable into the central nervous system
INVENTOR(S): Arvantis, Argyrios; Cain, Gary Avonn; Christos, Thomas Eugene; Confalone, Pasquale Nicholas; Pottorf, Richard Scott; Schmidt, William Koch
PATENT ASSIGNEE(S): Du Pont Merck Pharmaceutical Co., USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

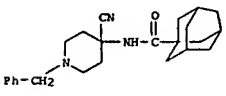
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9300359	A1	19930107	WO 1992-US4968	19920618
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9222381	A	19930125	AU 1992-22381	19920618
PRIORITY APPLN. INFO.:			US 1991-723616 A	19910627
			WO 1992-US4968 A	19920618

OTHER SOURCE(S): MARPAT 119:203857

AB YWmXnA1-H-A-B-C-D-E-F-Z [Y = lipophilic moiety LCO, R(CH2)p (O(CH2)r; p, r = 0-6; L = (substituted) alkyl, perfluoroalkyl, cycloalkyl, bicycloalkyl, tricycloalkyl, etc.; R = cycloalkyl, heterocyclyl, (substituted) aryl; W = Arg, D-Arg, D-Lys, Pro, Nle, Lys, Orn, homoarginine, 2,4-diaminobutyric acid, 2,3-diaminopropionic acid, N-methylnorleucine, 4-aminocyclohexylalanine residues; X = W, Ala, etc.; m, n = 0,1; A, A1, C, E = CONH, CONMe, NMeCO, CH2NH, CH2O, CH2S, CSNH, NHCONH, SOCH2, SO2CH2, NHSC, CH:CH, CH2CH2, CF2CF2, CF:CF, CF:CH, CH2CH(OH), cyclopropylene, 4,5-tetrazolyldiyl, etc.; H = Pro, N-methylaminobutyric acid residue; B = Tyr, Phe, Trp, naphthylalanine, phenylglycine, β-phenylproline residues; D = Ile, Leu, tert-leucine, phenylglycine residues; F = Leu, Val, Met; Z = OH, alkoxy], were prepared Thus, Q-Arg-Pro-Tyr-Ile-Leu-OH.HOAC (Q = 1-adamantanecarbonyl), prepared by solid phase coupling on phenylacetamidomethyl resin using BOC-protected amino acids and DCC/1-hydroxybenzotriazole, showed Ki = 144 nM in a neurotensin binding assay and ED50 = 14 mg/kg i.v. in the phenylquinone writhing test in mice.

IT 150463-82-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for neurotensin analog)

RN 150463-82-4 CAPLUS
CN Tricyclo[3.3.1.13,7]decane-1-carboxamide, N-[4-cyano-1-(phenylmethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



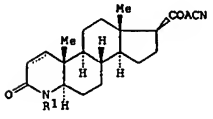
L11 ANSWER 55 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1993:539600 CAPLUS
DOCUMENT NUMBER: 119:139600
TITLE: Preparation and formulation of 3-oxo-4-aza-5α-androst(-1-ene)-17β-carboxamides and analogs as testosterone 5α-reductase inhibitors
INVENTOR(S): Biollaz, Michel
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 538192	A1	19930421	EP 1992-810766	19921008
EP 538192	B1	19970423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5304562	A	19940419	US 1992-954081	19920930
IL 103361	A	19970610	IL 1992-103361	19921005
CA 2080054	A1	19930410	CA 1992-2080054	19921007
AU 9226261	A	19930422	AU 1992-26261	19921007
AU 657579	B2	19950316		
NO 9203911	A	19930413	NO 1992-3911	19921008
ZA 9207747	A	19930413	ZA 1992-7747	19921009
HU 62600	A2	19930528	HU 1992-3189	19921008
AT 152121	T	19970515	AT 1992-810766	19921008
ES 2101073	T3	19970701	ES 1992-810766	19921008
JP 05213989	A	19930824	JP 1992-271226	19921009
US 5378710	A	19950103	US 1993-132399	19931006
PRIORITY APPLN. INFO.:			CH 1991-2978 A	19911009
			US 1992-954081 A1	19920930

OTHER SOURCE(S): MARPAT 119:139600

GI



I

AB Title compds. [I; A = NR2X, NR2YZ, OX, OYZ; R1 = H, Me, Et; R2 = H, alkyl; X = C1-2 alkylene, C3-6 cycloalkylidene; Y = bond, C1-6 alkylene; Z = (substituted) phenylene; dashed line = optional bond] were prepared as testosterone 5α-reductase inhibitors (no data). Thus, 3-oxo-4-aza-5α-androstane-17β-carboxylic acid was converted to the acid chloride which was condensed with 4-(H2N)C6H4CN to give N-(4-cyanophenyl)-3-oxo-4-aza-5α-androstane-17β-carboxamide.

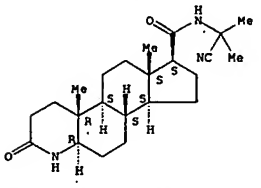
IT 149281-14-1P 149281-19-6P 149281-20-9P
149281-21-0P 149281-22-1P 149281-23-2P
149281-24-3P 149281-25-4P 149281-26-5P
149281-31-2P

Karen Cheng

L11 ANSWER 55 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as testosterone reductase inhibitor)

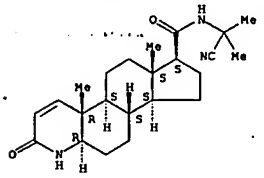
RN 149281-14-1 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-methylethyl)hexadecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 149281-19-6 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-methylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

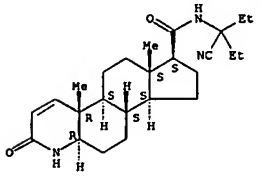
Absolute stereochemistry.



RN 149281-20-9 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-methylethyl)hexadecahydro-1,4a,6a-trimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

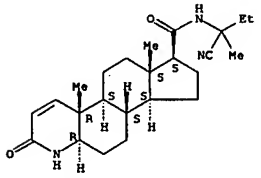
Absolute stereochemistry.

L11 ANSWER 55 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



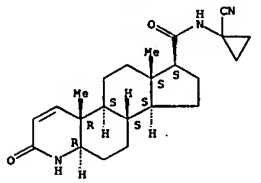
RN 149281-23-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-methylpropyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



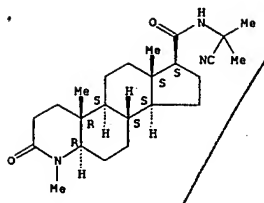
RN 149281-24-3 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyanocyclopropyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



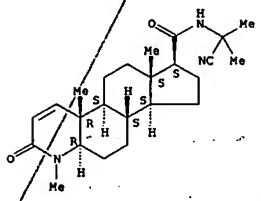
RN 149281-25-4 CAPLUS

L11 ANSWER 55 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 149281-21-0 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-methylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-1,4a,6a-trimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

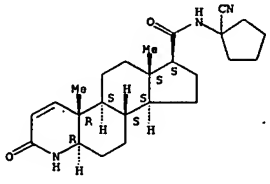


RN 149281-22-1 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-ethylpropyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

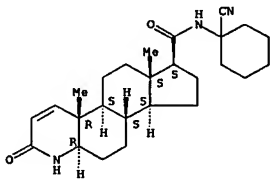
L11 ANSWER 55 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyanocyclopentyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 149281-26-5 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyanocyclohexyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-4a,6a-dimethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

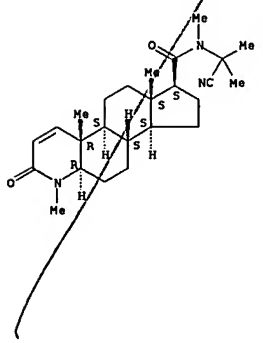


RN 149281-31-2 CAPLUS
CN 1H-Indeno[5,4-f]quinoline-7-carboxamide, N-(1-cyano-1-methylethyl)-2,4a,4b,5,6,6a,7,8,9,9a,9b,10,11,11a-tetradecahydro-N,1,4a,6a-tetramethyl-2-oxo-, (4aR,4bS,6aS,7S,9aS,9bS,11aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10560672restrict

L11 ANSWER 55 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L11 ANSWER 56 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

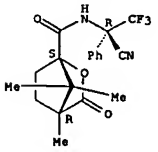
ACCESSION NUMBER: 1993:254501 CAPLUS
DOCUMENT NUMBER: 118:254501
TITLE: α-Amino-α-trifluoromethylphenylacetonitril e: a potential reagent for fluorine-19 NMR determination of enantiomeric purity of acids
AUTHOR(S): Kaos, Miroslav; Mosher, Harry S.
CORPORATE SOURCE: Dep. Chem., Stanford Univ., Stanford, CA, 94305, USA
SOURCE: Tetrahedron (1993), 49(8), 1541-6
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 118:254501

AB α-Amino-α-(trifluoromethyl)phenylacetonitrile, PhC(CF3)(CN)NH2, 2, in which the amino group is located on a crowded, chiral, quaternary carbon center, was studied as a potential reagent for the 19F NMR determination of enantiomeric purity of chiral acids by conversion to their corresponding diastereomeric amides. The differences in the 19F NMR chemical shifts (Δδ) of the R,R/S,S vs. R,S/S,R diastereomeric amides prepared from amine 2 and ten chiral acids range up to 0.266 ppm. Eight of the ten examples have Δδ in excess of the useful min. of 0.02 ppm. These values are not notably superior to those of other known reagents.

IT 147848-18-8P 147921-37-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and fluorine-19 NMR of)

RN 147848-18-8 CAPLUS
CN 2-Oxabicyclo[2.2.1]heptane-1-carboxamide, N-(1-cyano-2,2,2-trifluoro-1-phenylethyl)-4,7,7-trimethyl-3-oxo-, [1S-[1α(S*),4β]]- (9CI) (CA INDEX NAME)

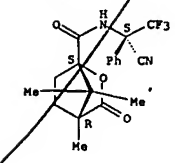
Absolute stereochemistry.



RN 147921-37-7 CAPLUS
CN 2-Oxabicyclo[2.2.1]heptane-1-carboxamide, N-(1-cyano-2,2,2-trifluoro-1-phenylethyl)-4,7,7-trimethyl-3-oxo-, [1S-[1α(R*),4β]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L11 ANSWER 56 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



L11 ANSWER 57 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

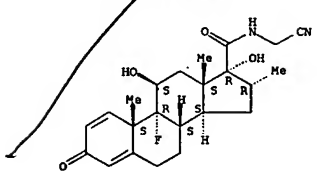
ACCESSION NUMBER: 1991:442143 CAPLUS
DOCUMENT NUMBER: 115:42143
TITLE: Hormones and antihormones. The steroidal model
AUTHOR(S): Formstecher, P. A.; Lefebvre, P.; Burollaud, T.
CORPORATE SOURCE: Lab. Biochim. Struct., Fac. Med., Lille, 59045, Fr.
SOURCE: Journal de Pharmacie de Belgique (1991), 46(1), 37-48
CODEN: JPBEAJ; ISSN: 0047-2166
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French

AB Structure activity relationships of a series of 17β-carboxamide derivs. of dexamethasone are described. The affinity of these compds. for the glucocorticoid receptor depends on the nature of the 17β-side chain substituent. An effect is observed at a rather large distance from the steroid nucleus. Maximal affinity is obtained with aromatic substituents. Antiglucocorticoid activity seems to be correlated with a high dissociation rate constant of the steroid receptor complexes and probably excludes the existence of a very active antiglucocorticoid in these series. Dexamethasone 17β-carboxamide derivs. share with all other antiglucocorticoids tested the same ability to stabilize a high mol. form of the receptor associated to HSP90, a heat shock protein, in intact cells. These data were accompanied by a review of recent findings on antiglucocorticoids and their action mechanism.

IT 116915-37-8
RL: BIOL (Biological study)
(antiglucocorticoid activity and hydrophobicity of, mol. structure in relation to)

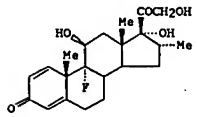
RN 116915-37-8 CAPLUS
CN Androsta-1,4-diene-17-carboxamide, N-(cyanomethyl)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxo-, (11β,16α,17α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Karen Cheng

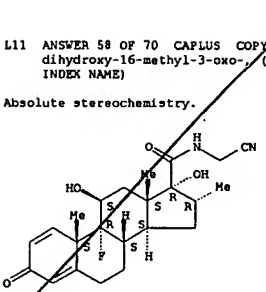
L11 ANSWER 58 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:48892 CAPLUS
DOCUMENT NUMBER: 112:48892
TITLE: Improvement in glucocorticoid receptor binding affinity concomitant to shift from antagonist to agonist activity in a series of 17β-carboxamide derivatives of dexamethasone
AUTHOR(S): Lefebvre, Philippe; Formstecher, Pierre; Rousseau, Guy G.; Lustenberger, P.; Dautrevaux, Michel
CORPORATE SOURCE: Lab. Biochim. Struct., Fac. Med., Lille, 59045, Fr.
SOURCE: Journal of Steroid Biochemistry (1989), 33(4A), 557-63
CODEN: JSTBBK; ISSN: 0022-4731
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Modification of the 17β-side chain of the synthetic glucocorticoid agonist dexamethasone (I) by periodic oxidation and subsequent coupling to various primary amines yield secondary 17β-carboxamide derivs. displaying antiglucocorticoid activity in vitro, but not in vivo. To obtain more potent antiglucocorticoids, new secondary and tertiary 17β-carboxamide derivs. were synthesized. Although they displayed an improved affinity for the glucocorticoid receptor in rat thymus cytosol and antiglucocorticoid activity in rat hepatoma (HTC) cells, these new compds. were again devoid of in vivo antiglucocorticoid activity in the rat. Moreover, the increase in receptor binding affinity was correlated for most compds. with the appearance of a partial agonist activity in HTC cells. The tertiary 17β-carboxamide derivative I diMe displayed the highest affinity but was also a partial agonist in vivo. Kinetic studies with several tritiated 17β-carboxamide derivs. showed that they had association rate consts. similar to that of I, but different dissociation rate consts. The rapid dissociation of the compds. displaying antiglucocorticoid activity contrasted with the slow dissociation of I diMe. Therefore, antiglucocorticoid activity in the 17β-carboxamide series is probably related to the formation of rapidly dissociating glucocorticoid receptor-ligand complexes that are unable to undergo the transformation step.
IT 116915-37-8
RL: BIOL (Biological study)
(biol. activity and glucocorticoid receptor binding by, structure in relation to)
RN 116915-37-8 CAPLUS
CN Androsta-1,4-diene-17-carboxamide, N-(cyanomethyl)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxo-, (11β,16α,17α)- (9CI) (CA INDEX NAME)

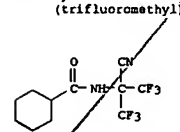
Absolute stereochemistry.



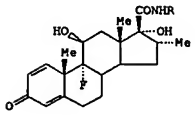
L11 ANSWER 59 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:585489 CAPLUS
DOCUMENT NUMBER: 109:185489
TITLE: Preparation of acylaminonitriles as insecticides, acaricides and herbicides
INVENTOR(S): Burger, Klaus; Huber, Erasmus; Ganzer, Michael; Puttner, Reinhold; Arndt, Friedrich; Joppien, Hartmut
PATENT ASSIGNEE(S): Schering A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3704100	A1	19880818	DE 1987-3704100	19870206
PRIORITY APPLN. INFO.:			DE 1987-3704100	19870206

OTHER SOURCE(S): CASREACT 109:185489; MARPAT 109:185489
AB The acylaminonitriles RCONHC(CF3)2CN [I; R = H, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, Ph, etc.] were prepared 3,4-C12C6H3CON:C(CF3)2 was heated, at 80°, with Me3SiCN, in toluene, for 80°, to give an intermediate, which was hydrolyzed with HCl, to give I (R = 3,4-C12C6H3) (II). II (0.0064%) totally controlled Plutella xylostella on Brassica oleracea botrytis leaves, in the laboratory
IT 117283-44-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as herbicide and insecticide)
RN 117283-44-0 CAPLUS
CN Cyclohexanecarboxamide, N-[1-cyano-2,2,2-trifluoro-1-(trifluoromethyl)ethyl]- (9CI) (CA INDEX NAME)



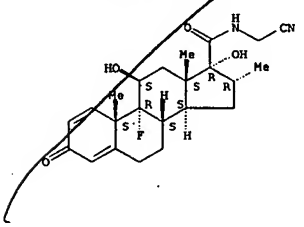
L11 ANSWER 60 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:563648 CAPLUS
DOCUMENT NUMBER: 109:163648
TITLE: High-performance liquid chromatography in the evaluation of the lipophilicity of 17β-carboxamide steroid derivatives
AUTHOR(S): Maes, P.; Formstecher, P.; Lustenberger, P.; Dautrevaux, M.
CORPORATE SOURCE: Lab. Biochim. Struct., Fac. Med., Lille, 59045, Fr.
SOURCE: Journal of Chromatography (1988), 445(2), 409-16
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Octanol-phosphate buffer partition coeffs. as an expression of lipophilicity of 38 dexamethasone carboxamide derivs. (I, R = H, alkyl, phenylalkyl, amino- or carboxyalkyl, etc) were correlated with log k' (capacity factors) measured directly by reversed-phase HPLC. These log k' values can thus be used to establish QSAR between chromatog. retention parameters of steroids and the dissociation constant of complexes formed with the glucocorticoid receptor.
IT 116915-37-8
RL: BIOL (Biological study)
(HPLC retention correlation with lipophilicity of, QSAR in relation to)
RN 116915-37-8 CAPLUS
CN Androsta-1,4-diene-17-carboxamide, N-(cyanomethyl)-9-fluoro-11,17-dihydroxy-16-methyl-3-oxo-, (11β,16α,17α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



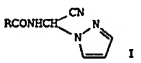
L11 ANSWER 60 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L11 ANSWER 61 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:496717 CAPLUS
DOCUMENT NUMBER: 107:96717
TITLE: A process for the preparation of (acylamino)pyrazolylacetonitriles and agricultural fungicides and herbicides containing them
INVENTOR(S): Ishii, Tsutomu; Tanaka, Yoshinori; Shimotori, Hitoshi; Nishida, Makoto; Hojo, Sachoshi
PATENT ASSIGNEE(S): Mitsui Toatsu Chemicals, Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62103067	A	19870513	JP 1985-240665	19851029
PRIORITY APPLN. INFO.:			JP 1985-240665	19851029

GI

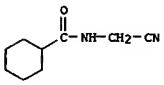


I

AB The title compds. (I; R = alkyl, alkenyl, alkoxyalkyl, cycloalkyl, haloalkyl, haloalkenyl, halocycloalkyl), useful as agricultural fungicides and herbicides for a rice paddy, were prepared [(Cyclohexylcarbonyl)amino]acetonitrile was brominated in EtOAc, followed by dropwise addition of a solution of pyrazole and Et3N in THF. The mixture was allowed to react for an addnl. 0.5 h at 0-5° to give 76.9% I (R = cyclohexylcarbonyl). In postemergence treatment, the latter gave 95-100% control of Echinochloa crus-galli.

IT 35970-22-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(bromination and amination of, by pyrazole)

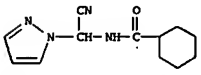
RN 35970-22-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyanomethyl)- (9CI) (CA INDEX NAME)



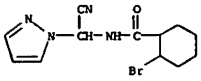
IT 110023-30-8P 110023-31-9P 110023-32-0P
110023-40-0P 110023-44-4P

L11 ANSWER 61 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as herbicide and agrochem. fungicide)

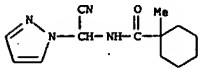
RN 110023-30-8 CAPLUS
CN Cyclohexanecarboxamide, N-(cyano-1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



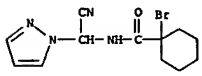
RN 110023-31-9 CAPLUS
CN Cyclohexanecarboxamide, 2-bromo-N-(cyano-1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



RN 110023-32-0 CAPLUS
CN Cyclohexanecarboxamide, N-(cyano-1H-pyrazol-1-ylmethyl)-1-methyl- (9CI) (CA INDEX NAME)

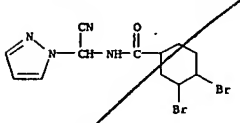


RN 110023-40-0 CAPLUS
CN Cyclohexanecarboxamide, 1-bromo-N-(cyano-1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)



RN 110023-44-4 CAPLUS
CN Cyclohexanecarboxamide, 3,4-dibromo-N-(cyano-1H-pyrazol-1-ylmethyl)- (9CI) (CA INDEX NAME)

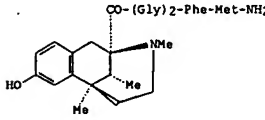
L11 ANSWER 61 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



Karen Cheng

10560672restrict

L11 ANSWER 62 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:593266 CAPLUS
DOCUMENT NUMBER: 97:193266
TITLE: Synthesis and biological evaluation of a metazocine-containing enkephalinamide. Evidence for nonidentical roles of the tyramine moiety in opiates and opioid peptides
AUTHOR(S): Ramakrishnan, K.; Portoghese, P. S.
CORPORATE SOURCE: Coll. Pharm., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Journal of Medicinal Chemistry (1982), 25(12), 1423-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

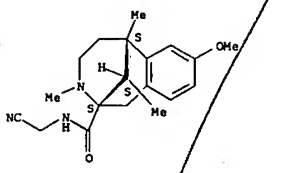


I

AB The title compound (-)-(2R,6R,11R)-[(1,2,3,4,5,6-hexahydro-8-hydroxy-3,6,11-trimethyl-2,6-methano-3-benzazocin-2-yl)carbonyl]glycylglycylphenylalanylmethioninamide (I) [83380-08-9] prepared by coupling (-)-(2α,6α,11α)-[(1,2,3,4,5,6-hexahydro-8-hydroxy-3,6,11-trimethyl-2,6-methano-3-benzazocin-2-yl)carbonyl]glycine [83435-02-3] with glycylphenylalanylmethioninamide-HCl [75189-51-4], and some of its congeners were evaluated in elec. stimulated myenteric plexus of guinea pig ileum and mouse vas deferens to test the hypothesis that the tyramine moiety present in opiates and in opioid peptides plays an identical functional role at opioid receptors. The results indicate that the tyramine moiety of morphine-related structures and enkephalin do not play identical roles in the interaction with opioid receptors.
IT 83380-06-7P 83435-00-1P 83435-01-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and acidification of)
RN 83380-06-7 CAPLUS
CN 2,6-Methano-3-benzazocine-2(1H)-carboxamide, N-(cyanomethyl)-3,4,5,6-tetrahydro-8-methoxy-3,6,11-trimethyl-, (2α,6β,11R*)- (9CI) (CA INDEX NAME)

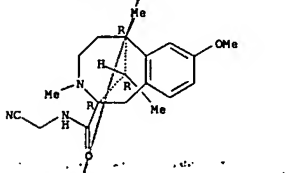
Relative stereochemistry.

L11 ANSWER 62 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



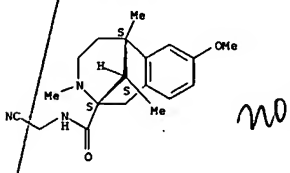
RN 83435-00-1 CAPLUS
CN 2,6-Methano-3-benzazocine-2(1H)-carboxamide, N-(cyanomethyl)-3,4,5,6-tetrahydro-8-methoxy-3,6,11-trimethyl-, [2R-(2α,6β,11R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



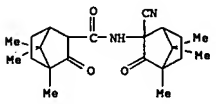
RN 83435-01-2 CAPLUS
CN 2,6-Methano-3-benzazocine-2(1H)-carboxamide, N-(cyanomethyl)-3,4,5,6-tetrahydro-8-methoxy-3,6,11-trimethyl-, [2S-(2α,6β,11R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



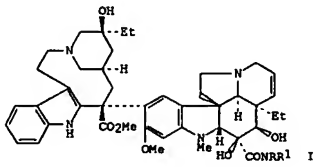
no fused rings.

L11 ANSWER 63 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:419465 CAPLUS
DOCUMENT NUMBER: 91:19465
TITLE: Voltammetric study of the anodic oxidation of enolate carbanions
AUTHOR(S): Kern, Jean Marc; Federlin, Paul
CORPORATE SOURCE: Inst. Chim., Univ. Louis Pasteur, Strasbourg, 67000, Fr.
SOURCE: Journal of Electroanalytical Chemistry and Interfacial Electrochemistry (1978), 96(2), 209-28
CODEN: JEIEBC; ISSN: 0022-0728
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A voltammetric study of the anodic oxidation of the enolate carbanions of β-ketonitriles RCH(CN)COR1 has been carried out in Me2SO. The variation of Eox of these species as a function of the nature of R and R1 was examined Their anodic oxidation process could be identified by anal. of the voltamperometric curves obtained both at the rotated Pt electrode and at the stationary electrode. Cyclic voltammetry has confirmed that this is an ec overall irreversible process. The electrochem. reaction e yielding a neutral radical is followed by the very fast dimerization (2nd-order chemical reaction c). The formation of different kinds of dimers, depending on the nature of the oxidized enolates, has been observed during controlled potential electrolysis.
IT 70230-44-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 70230-44-3 CAPLUS
CN Bicyclo[2.2.1]heptane-2-carboxamide, N-(2-cyano-4,7,7-trimethyl-3-oxobicyclo[2.2.1]hept-2-yl)-4,7,7-trimethyl-3-oxo- (9CI) (CA INDEX NAME)

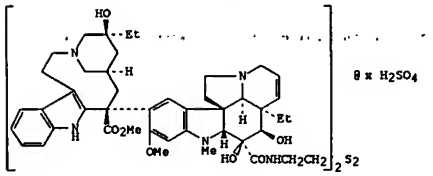


Karen Cheng

L11 ANSWER 64 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1979:179908 CAPLUS
DOCUMENT NUMBER: 90:179908
TITLE: Structure-activity relationships of dimeric Catharanthus alkaloids. 2. Experimental antitumor activities of N-substituted deacetylvinblastine amide (vindesine) sulfates
AUTHOR(S): Conrad, Robert A.; Cullinan, George J.; Gerzon, Koert; Poore, Gerald A.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, USA
SOURCE: Journal of Medicinal Chemistry (1979), 22(4), 391-400
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



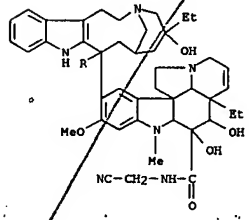
II

AB The synthesis and antitumor activities of 40 N-substituted vindesine [53643-48-4] analogs I (R = H or Me; R1 = Me, CH2CN, CH2CH2SH, etc.) are described. I were synthesized by reaction of deacetylvinblastine acid azide [55324-86-2] with appropriate amines. I; R = H, R1 = CH2CH2OH.xH2SO4 [55324-80-6] was superior in suppressing the growth of Gardner lymphosarcoma and Ridgway osteogenic sarcoma but was less active against B16 melanoma than vindesine in mice. In terms of collective antitumor activity against the model systems used, vindesine had optimum quantities. II [66791-70-6] had a comparable antitumor activity profile to vindesine and had activity against a P388/VCR leukemia strain resistant

L11 ANSWER 64 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
to maytansine and vincristine. Structure-activity relations are discussed.
IT 55324-82-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of)
RN 55324-82-8 CAPLUS
CN Vincaleukoblastine, 3-[[(cyanomethyl)amino]carbonyl]-O4-deacetyl-3-de(methoxycarbonyl)-, sulfate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 55324-81-7
CMF C45 H56 N6 O7



CM 2

CRN 7664-93-9
CMF H2 O4 S

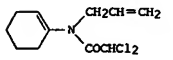
L11 ANSWER 65 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1977:579027 CAPLUS
DOCUMENT NUMBER: 87:179027
TITLE: Herbicide antidotes
INVENTOR(S): Pallos, Ferenc M.; Brokke, Mervin E.; Arneklev, Duane R.
PATENT ASSIGNEE(S): Stauffer Chemical Co., USA
SOURCE: U.S., 46 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4021224	A	19770503	US 1975-641783	19751217
US 4137070	A	19790130	US 1971-208041	19711209
CA 1174865	A1	19840925	CA 1972-139060	19720406
NL 7204894	A	19721018	NL 1972-4894	19720412
NL 175965	B	19840903		
NL 175965	C	19850201		
OD 102075	A5	19731212	DD 1972-162258	19720412
OK 143583	B	19810914	DK 1972-1773	19720412
DK 143583	C	19820201		
CS 196241	B2	19800331	CS 1972-2480	19720413
BE 782120	A1	19721016	BE 1972-116328	19720414
FR 2133793	A5	19721201	FR 1972-13316	19720414
FR 2133793	B1	19770624		
ZA 7202519	A	19730131	ZA 1972-2519	19720414
BR 7202240	DO	19730503	BR 1972-2240	19720414
AU 7241186	A	19731018	AU 1972-41186	19720414
IL 39219	A	19781217	IL 1972-39219	19720414
DE 2266035	C2	19871029	DE 1972-2266035	19720414
IT 953649	B	19730810	IT 1972-23209	19720415
ES 401779	A1	19751101	ES 1972-401779	19720415
GB 1396941	A	19750611	GB 1972-14754	19720416
GB 1396942	A	19750611	GB 1974-54475	19720416
CH 577785	A5	19760730	CH 1972-5637	19720417
RO 78996	A1	19820625	RO 1972-70563	19720417
RO 83875	A1	19840402	RO 1972-108380	19720417
RO 83877	A1	19840402	RO 1972-108381	19720417
DK 7503225	A	19751020	DK 1975-3225	19750715
DK 141231	B	19800211		
DK 141231	C	19800728		
DK 7503224	A	19751103	DK 1975-3224	19750715
OK 136231	B	19770912		
US 4124372	A	19781107	US 1976-710503	19760802
DK 7604782	A	19761022	DK 1976-4782	19761022
OK 141712	B	19800602		
DK 141712	C	19801027		
US 4124376	A	19781107	US 1977-759687	19770117
US 4269618	A	19810526	US 1978-930967	19780804
US 4276078	A	19810630	US 1979-49767	19790618
US 4341550	A	19820727	US 1979-55578	19790709
US 4392884	A	19830712	US 1980-147434	19800507
US 4519833	A	19850528	US 1981-292330	19810813
US 4517012	A	19850514	US 1982-363673	19820330
US 4415352	A	19831115	US 1982-369322	19820416
US 4415353	A	19831115	US 1982-441963	19821115

L11 ANSWER 65 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

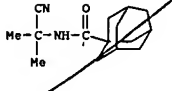
US 4708735	A	19871124	US 1984-640287	19840813
US 4971618	A	19901120	US 1986-850424	19860407
PRIORITY APPLN. INFO.:			US 1971-134868	A2 19710416
			US 1971-208041	A3 19711209
			DK 1972-1773	A 19720412
			US 1972-297561	A2 19721013
			US 1973-356547	A3 19730502
			US 1975-641783	A3 19751217
			US 1978-930967	A3 19780804
			US 1979-55578	A3 19790709
			US 1980-147434	A3 19800507
			US 1980-196517	B3 19801014
			US 1980-196518	A3 19801014
			US 1982-369322	A3 19820416
			US 1983-480185	A3 19830328

OTHER SOURCE(S): MARPAT 87:179027
GI



I

AB Plant protection against injury by herbicides is obtained by addition to the soil or crop seed of an antidote RCONR1R2 (R = haloalkyl, alkyl, cycloalkyl, halogen, H, etc.; R1 and R2 can be the same or different and = H, alkyl, alkynyl, NH2, Ph, etc., or NR1R2 = piperidinyl, oxazolidyl, etc.). Thus, in greenhouse tests, 10 g corn seed treated with 50 mg I [39085-02-4] and planted in EPTC [759-94-4]-treated soil (6 lb/A) showed no injury after 2 and 4 weeks compared to 55 and 60% injury, resp., for the untreated controls. The syntheses of the antidote compds. are given.
IT 39106-30-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and herbicidal antidote activity of)
RN 39106-30-4 CAPLUS
CN Tricyclo[3.3.1.13,7]decane-1-carboxamide, N-(1-cyano-1-methylethyl)- (9CI) (CA INDEX NAME)



Karen Cheng

L11 ANSWER 66 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1975:57996 CAPLUS
DOCUMENT NUMBER: 82:57996
TITLE: Amine derivatives of vinblastine, leurosidine and leurocristine
INVENTOR(S): Cullinan, George J.; Gerzon, Koert
PATENT ASSIGNEE(S): Eli Lilly and Co.
SOURCE: Ger. Offen., 40 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2415980	A1	19741010	DE 1974-2415980	19740402
DE 2415980	C2	19891109		
ZA 7401674	A	19751029	ZA 1974-1674	19740313
IL 44415	A	19780831	IL 1974-44415	19740313
AU 7466719	A	19750918	AU 1974-66719	19740315
CA 1042428	A1	19781114	CA 1974-195760	19740322
GB 1463575	A	19770202	GB 1974-13101	19740325
FR 2223044	A1	19741025	FR 1974-11519	19740329
FR 2223044	B1	19780630		
CH 603669	A5	19780831	CH 1974-4463	19740329
NL 7404423	A	19741004	NL 1974-4423	19740401
NL 181079	B	19870116		
NL 181079	C	19870616		
AT 7402679	A	19770415	AT 1974-2679	19740401
AT 340605	B	19771227		
CS 185223	B2	19780915	CS 1974-2335	19740401
AT 345996	B	19781010	AT 1975-9801	19740401
DK 141511	B	19800408	DK 1974-1787	19740401
DK 141511	C	19800929		
SU 731900	A3	19800430	SU 1974-2013753	19740401
SE 416206	B	19801208	SE 1974-4380	19740401
SE 416206	C	19810326		
BE 813168	A1	19741002	BE 1974-1005847	19740402
JP 49128000	A	19741207	JP 1974-37765	19740402
JP 59019117	B	19840502		
DD 113538	A5	19750612	DD 1974-177632	19740402
ES 424882	A1	19761216	ES 1974-424882	19740402
RO 77533	A1	19820201	RO 1974-98695	19740402
RO 73524	A1	19841031	RO 1974-78274	19740402
SU 784783	A3	19801130	SU 1975-2151512	19750704
SU 652896	A3	19790315	SU 1975-2152020	19750709
ES 446571	A1	19770616	ES 1976-446571	19760331
SU 623522	A3	19780905	SU 1976-2429453	19761220
US 4203898	A	19800520	US 1978-954514	19781025
US 4479957	A	19841030	US 1981-250459	19810402
JP 59193895	A	19841102	JP 1983-238722	19831216
JP 60033837	B	19850805		

PRIORITY APPLN. INFO.:

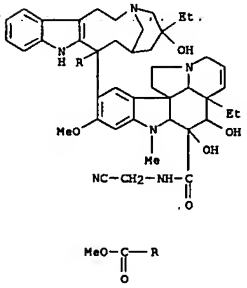
US 1973-347275	A	19730402
US 1974-446869	A2	19740228
AT 1974-2679	A	19740401

L11 ANSWER 66 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
US 1975-539681 A2 19750109
US 1976-721650 A2 19760908
US 1977-828693 A1 19770829
US 1978-935828 A2 19780822
US 1979-101335 A1 19791206

GI For diagram(s), see printed CA Issue.
AB Amides of vinblastine I (R = HO, R1 = H, R2 = Me, R3 = H2N, MeNH, EtNH, H2NNH, HOCH2CH2NH, Me2N, NCCH2CH2NH, Me2CHNH, Me2NCH2CH2NH; R4 = H, Ac) leurosidine I (R = H, R1 = HO, R2 = Me, R3 = H2N, H2NNH; R4 = H), and leurocristine I (R = HO, R1 = H, R2 = H, HCO; R3 = MeNH, H2N, EtNH, R4 = H) and their sulfate salts (23 compds.), which inhibited tumors in mice, were prepared by treating the title compds. with R3H in anhydrous MeOH. Thus,
MeNH2 in anhydrous MeOH was treated with vinblastine and the mixture was stored
for 8 days at 50° to give a mixture of I (R1 = H, R2 = Me, R3 = MeNH, R4 = H, Ac) which was treated with Ac2O and pyridine to give I (R4 = Ac) or was separated chromatog. into I (R4 = H) and I (R4 = Ac).
IT 55324-82-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and carcinostatic activity of)
RN 55324-82-8 CAPLUS
CN Vincaleukoblastine, 3-[[(cyanomethyl)amino]carbonyl]-O4-deacetyl-3-de(methoxycarbonyl)-, sulfate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 55324-81-7
CMF C45 H56 N6 O7

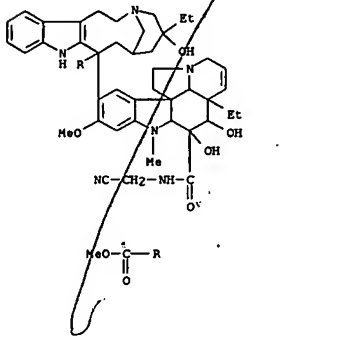


CM 2

L11 ANSWER 66 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CRN 7664-93-9
CMF H2 O4 S

IT 55324-81-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 55324-81-7 CAPLUS
CN Vincaleukoblastine, 3-[[(cyanomethyl)amino]carbonyl]-O4-deacetyl-3-de(methoxycarbonyl)- (9CI) (CA INDEX NAME)



L11 ANSWER 67 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:29282 CAPLUS
DOCUMENT NUMBER: 78:29282
TITLE: Culture plant protecting carbamoyl compounds
INVENTOR(S): Pallos, Ferenc Marcus; Brokke, Mervin Edward; Arnekley, Duane Randall
PATENT ASSIGNEE(S): Stauffer Chemical Co.
SOURCE: Ger. Offen., 168 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2218097	A1	19721102	DE 1972-2218097	19720414
DE 2218097	C2	19870730		
US 4137070	A	19790130	US 1971-208041	19711209
CA 1174865	A1	19840925	CA 1972-139060	19720406
NL 7204894	A	19721018	NL 1972-4894	19720412
NL 175965	B	19840903		
NL 175965	C	19850201		
DD 102075	A5	19731212	DD 1972-162258	19720412
DK 143583	B	19810914	DK 1972-1773	19720412
DK 143583	C	19820201		
CS 196241	B2	19800331	CS 1972-2480	19720413
BE 782120	A1	19721016	BE 1972-116328	19720414
FR 2133793	A5	19721201	FR 1972-13316	19720414
FR 2133793	B1	19770624		
ZA 7202519	A	19730131	ZA 1972-2519	19720414
BR 7202240	D0	19730503	BR 1972-2240	19720414
AU 7241186	A	19731018	AU 1972-41186	19720414
IL 39219	A	19781217	IL 1972-39219	19720414
DE 2266035	C2	19871029	DE 1972-2266035	19720414
IT 953649	B	19730810	IT 1972-23209	19720415
ES 401779	A1	19751101	ES 1972-401779	19720415
GB 1396941	A	19750611	GB 1972-14754	19720416
GB 1396942	A	19750611	GB 1974-54475	19720416
CH 577785	A5	19760730	CH 1972-5637	19720417
RO 78996	A1	19820625	RO 1972-70563	19720417
RO 83875	A1	19840402	RO 1972-108380	19720417
RO 83877	A1	19840402	RO 1972-108381	19720417
DK 7503225	A	19751020	DK 1975-3225	19750715
DK 141231	B	19800211		
DK 141231	C	19800728		
DK 7503224	A	19751103	DK 1975-3224	19750715
DK 136231	B	19770912		
US 4124372	A	19781107	US 1976-710503	19760802
DK 7604782	A	19761022	DK 1976-4782	19761022
DK 141712	B	19800602		
DK 141712	C	19801027		
US 4269618	A	19810526	US 1978-930967	19780804
US 4276078	A	19810630	US 1979-49767	19790618
US 4341550	A	19820727	US 1979-55578	19790709
US 4392884	A	19830712	US 1980-147434	19800507
US 4519833	A	19850528	US 1981-292330	19810813
US 4517012	A	19850514	US 1982-363673	19820330
US 4415352	A	19831115	US 1982-369322	19820416
US 4415353	A	19831115	US 1982-441963	19821115

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L11 ANSWER 67 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

US 4708735	A	19871124	US 1984-640287		19840813
US 4971618	A	19901120	US 1986-850424		19860407
PRIORITY APPLN. INFO.:			US 1971-134868	A	19710416
			US 1971-208041	A	19711209
			DK 1972-1773	A	19720412
			US 1972-297561	A2	19721013
			US 1973-356547	A3	19730502
			US 1978-930967	A3	19780804
			US 1979-55578	A3	19790709
			US 1980-147434	A3	19800507
			US 1980-196517	B3	19801014
			US 1980-196518	A3	19801014
			US 1982-369322	A3	19820416
			US 1983-480185	A3	19830328

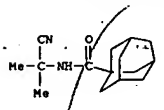
OTHER SOURCE(S): CASREACT 78:29282

AB Forty-two title compds., RCONR1R2 (I; R = e.g. n-C9H19, ClCH2, NCSCH2, PhCH2, 1-adamantyl, or cyclopropyl; R1 = or R2 = e.g., H, alkyl, CH2CH:CH2, CMe2CN, alkynyl, furfuryl, or 2-pyridyl; or NR1R2 = e.g., piperidino or morpholino) were prepared by reaction of RCOCl with HNR1R2. Thus, HN(CH2CH:CH)2 was added to ClCHCOCl in CH2Cl2 at <10° and the mixture stirred 4 hr to give I (R = ClCH, R1 = R2 = CH2CH:CH2). Thirty-nine of these I and 474 similar I were used for the protection of culture plants, e.g. wheat and corn, against damage by herbicides.

IT 39106-30-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(plant protection by, from herbicidal damage)

RN 39106-30-4 CAPLUS

CN Tricyclo[3.3.1.13,7]decane-1-carboxamide, N-(1-cyano-1-methylethyl)- (9CI) (CA INDEX NAME)



L11 ANSWER 68 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

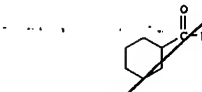
ACCESSION NUMBER: 1972:123358 CAPLUS
DOCUMENT NUMBER: 76:123358
TITLE: Proteolytic enzymes. Nature of binding forces between papain and its substrates and inhibitors
AUTHOR(S): Williams, A.; Lucas, E. C.; Rimmer, A. R.; Hawkins, H. C.
CORPORATE SOURCE: Univ. Chem. Lab., Univ. Kent, Canterbury, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 2: Physical Organic Chemistry (1972-1999) (1972), (5), 627-33
CODEN: JCPKBH; ISSN: 0300-9580
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The binding of papain to 20 substrates of the type RCONHCHR1COX, e.g. BzNHCH2CO2Me and PhCH2O2CNHCHMeCO2C6H4NO2-p, was shown by enzyme kinetics using the Michaelis-Menten relation to involve interaction between RCONH-, R1-, and -COX moieties, and complementary sites (ρ1, ρ2, and ρ3) on the enzyme. The ρ2 and ρ3 interactions involved lipophilic forces not of charge-transfer type, and the ρ2 interaction did not involve electrostatic forces but depended on the length of the side chain. Seventeen nonpeptide competitive inhibitors, e.g. R2CONHCH2CN (R2 = p-O2NC6H4, PhCH2O) or PhCH2NHBz were designed knowing the nature of ρ1 and ρ3.

IT 35970-22-0
RL: BIOL (Biological study)
(papain inhibition by)

RN 35970-22-0 CAPLUS

CN Cyclohexanecarboxamide, N-(cyanomethyl)- (9CI) (CA INDEX NAME)



L11 ANSWER 69 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1964:30901 CAPLUS
DOCUMENT NUMBER: 60:30901
ORIGINAL REFERENCE NO.: 60:5481a-c
TITLE: Synthetic studies involving 1-aminocyclohexanecarbonitrile
AUTHOR(S): Noland, Wayland E.; Sundberg, Richard J.; Michaelson, Margaret L.
CORPORATE SOURCE: Univ. of Minnesota, Minneapolis
SOURCE: Journal of Organic Chemistry (1963), 28(12), 3576-7
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

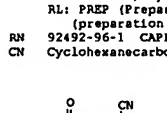
GI For diagram(s), see printed CA Issue.

AB A new heterocyclic dispiro compound, 7,14-diazadispiro[5.1.5.2]pentadecan-15-one (I), was prepared Cyclohexanecarbonyl chloride (44 g.) added dropwise to 32 g. 1-aminocyclohexanecarbonitrile (Ia) in 50 ml. C5H5N and 120 ml. C6H6, and the solution kept 12 hrs. in an unheated water bath, initially at 80°, and worked up gave 54.2 g. 1-(cyclohexanecarboxamido)-cyclohexanecarbonitrile (II), m. 163-4°. II (2.1 g.) and 0.2 g. NaNH2 heated 1 hr. at 180° (gas evolution began at 150°) and worked up gave 0.297 g. cyclohexanecarboxamide (III), m. 190-1°. II (2.1 g.) and 0.3 g. solid NaH refluxed 20 hrs. in 30 ml. C6H6, then refluxed 4 hrs. with 1 ml. alc., 1 ml. tert-BuOH, and 0.03 g. Na and evaporated, the residue partitioned between HCl and CHCl3, the CHCl3 layer evaporated, and the product sublimed in vacuo gave 0.103 g. III. Et cyclohexanone-2-carboxylate (IV) was obtainedin 59% yield from cyclohexanone, n28D 1.4762. p-MeC6H4SO3H (0.2 g.) refluxed 3 hrs. with 34 g. IV and 16.7 g. ethylene glycol in 100 ml. C6H6 gave 39.3 g. Et 1,4-dioxaspiro[4.5]decane-6-carboxylate (V), b1 95-104°, n28D 1.4632. Ia (20 g.) kept 20 hrs. at 90° or 40 hrs. at room temperature gave bis(1-cyanocyclohexyl)amine (VI), m. 137-8°. Attempted condensation of V with Ia gave 22% VI. Ia (21 g.) left 21 hrs. at room temperature with 2.8 g. Na in alc. gave 17.66 g. I, m. 219°. Infrared spectra were given for the above compds. Attempted condensation of Ia with IV gave .apprx.8% I. Repetition of the reaction in the absence of IV but in alc. containing a little moisture gave 94% I.

IT 92492-96-1P, Cyclohexanecarboxamide, N-(1-cyanocyclohexyl)-
RL: PREP (Preparation)
(preparation of)

RN 92492-96-1 CAPLUS

CN Cyclohexanecarboxamide, N-(1-cyanocyclohexyl)- (6CI, 7CI) (CA INDEX NAME)



L11 ANSWER 70 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1958:20826 CAPLUS
DOCUMENT NUMBER: 52:20826
ORIGINAL REFERENCE NO.: 52:3677i,3678a-e
TITLE: Properties and reactions of free alkyl radicals in solution. IX. Synthesis and reactions of some tertiary nitroalkanes
AUTHOR(S): Tilney-Bassett, J. F.; Waters, William A.
CORPORATE SOURCE: Univ. Oxford, UK
SOURCE: Journal of the Chemical Society (1957) 3129-34
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 50, 10005e. NO2 (9 g. containing a little N2O3) in 60 cc. dry C6H6 added over 0.5 hr. to 30 g. (:NCMe2CN)2 (I) in 200 cc. refluxing C6H6, and the mixture refluxed 5 hrs. and distilled in vacuo yields 7 g. Me2C(NO2)CN (II), m. 34° (Et2O). Chromatography of the distillation residue yields 10.8 g. (CMe2CN)2 (III), 2.3 g. NCCMe2ON(CMe2CN)2 (IV), and 0.4 g. Me2C(NO2)CONHCMe2CN, m. 135° (from C6H6). The same experiment with equal wts. (40 g.) of NO2 and I yields 31% II, 10% III, 1.7% IV, and 2.3% Me2C(NO2)CONHCMe2CO2H, m. 174° (CHCl3Me2CO). NO2 (5 g.) in C6H6 added slowly to 10.5 g. PhNO in refluxing C6H6 yields 67% PhNO2 and a tarry residue. Equal amts. of NO2 and (:NCMe2CO2Me)2 in PhMe at 100° yield 33% Me2C(NO2)CO2Me (V), b14 77-9°, m. -4°, also prepared from II via the corresponding HCl salt, m. 117°. V and saturated NH3-EtOH yield Me2C(NO2)CONH2, m. 116°. NO2 and (:NCEt2CN)2 in PhMe at 100° yield 21% O2NCMeEtCN (VI), b11 89-92°, 14% (Me2CCN)2, and 8% Et2C(NO2)CONHCEt2CN, m. 113.5°. Acid hydrolysis of VI yields 3-carbamoyl-3-nitropentane m. 59° (cyclohexane). NO2 and 1,1'-azobis(1-cyanocyclohexane) in boiling PhMe yield 24% 1-cyano-1-nitrocyclohexane (VII), m. 56°, 30% of the radical dimer, m. 223°, 3.6% N-(1-cyanocyclohexyl)cyclohexanecarboxamide, m. 156°, and 3.6% C21H32O4N4 (VIII), m. 145°. Decomposition of VIII in boiling PhCl yields VII. Hydrolysis of VII with strong H2SO4 yields 1-nitrocyclohexanecarboxyamide, m. 120°. Alkaline hydrolysis of II yields NaOCN as the major product although Me2CO and NO2 are obtained. Acidification of the solution yields CO2 and a blue color, presumably due to condensation of HNO2 and Me2C(NO)NO2. Thus although there is some SN2 displacement of NO2 by OH, the main hydrolytic reaction is HO + NCCR2NO2 → HOCN + (R2C:NO2). II (5 g.) and 2.5 g. NaCN refluxed overnight in 50 ml. dry EtOH, the EtOH distilled off, and H2O added to the residue yield 1.3 g. Me2C(CN)C(NO2)Me2, (IX), m. 194°, also prepared from II and (Me2CNO2)Na. II (3 g.) in 30 cc. dry Et2O added to a suspension of LiAlH4 in 50 cc. refluxing Et2O, H2O added after 1 hr., and the amine extracted with dilute acid, concentrated in salt form, and benzoylated yields 62% BzNHCHMe2 (X), m. 98°, also obtained from V. Similarly VII yields N-benzoylcyclohexylamine. V (2 g.) in 15 cc. MeOH refluxed with 1 g. Raney Ni, treated with 3 cc. aqueous N2H4, the mixture refluxed 30 min., filtered, acidified, concentrated, and benzoylated yields 1.3 g. Me2C(NHBz)CO2Me, m. 120°.

IT 92492-96-1P, Cyclohexanecarboxamide, N-(1-cyanocyclohexyl)-
RL: PREP (Preparation)
(preparation of)

RN 92492-96-1 CAPLUS

CN Cyclohexanecarboxamide, N-(1-cyanocyclohexyl)- (6CI, 7CI) (CA INDEX NAME)

Karen Cheng

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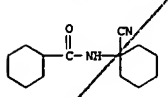
L11 ANSWER 70 OF 70 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



Karen Cheng